EXHIBIT 58 (part 2 of 2)

The statistical analysis examines the size of discounts offered on brand-name drugs after adjusting for the effects of the number of brand-name and generic competitors, the therapeutic class of the drug, and its Medicaid market share. (For more details of the analysis, see Appendix B.) The results show that the best-price discount on a brand-name drug is 10 to 14 percentage points greater when therapeutically similar brand-name drugs are available from three or more manufacturers. As more producers of brand-name drugs enter a particular therapeutic class, the size of the best-price discount increases. Similar increases occur when generic competitors enter a market. Those results confirm the theory that the steep discounts on brand-name drugs available to some purchasers are a response to competitive market conditions.[46]

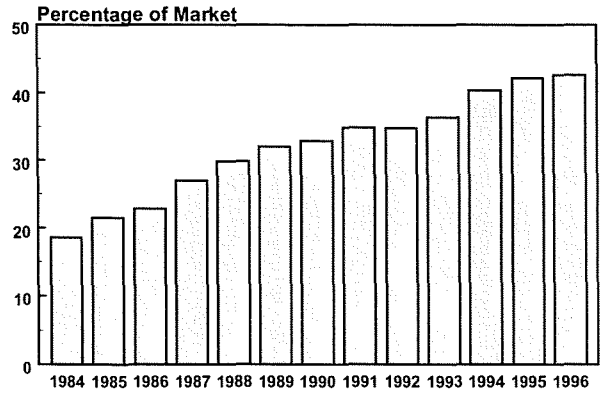
Competition Between Brand-Name and Generic Drugs

One of the primary goals of the Hatch-Waxman Act was to increase the availability of lower-cost generic drugs. Since the act became law in 1984, the market share of generic drugs has indeed been rising steadily—although not all of that increase stems from the act. For drugs that come in easily countable units, such as tablets and capsules, the share of generic units sold more than doubled between 1984 and 1996—from 18.6 percent of all drug units sold to 42.6 percent (see Figure 6).[47]

Those numbers are probably the best publicly available estimate documenting the rise in generic market share since 1984. However, since countable units do not include injectable drugs and many types of prescription drugs dispensed in liquid form, they are not a perfect measure of average generic market share. Many injectable drugs are dispensed primarily in hospitals and other inpatient settings, so the estimate may underrepresent those channels of distribution. Countable units appear to yield an estimate of generic market share similar to that measured by the number of prescriptions dispensed through retail pharmacies.[48]

The Hatch-Waxman Act encouraged the entry of generic drugs by establishing an abbreviated approval process for generic versions of all nonantibiotic drugs (antibiotics already had such a process). In addition, the act reversed a 1984 court ruling and allowed generic manufacturers to begin the tests required for

Figure 6.
Growth in the Market Share of Generic Drugs Since 1984



SOURCE: Pharmaceutical Research and Manufacturers of America, *1997 Industry Profile* (Washington, D.C.: PhRMA, March 1997), p. 40, based on data from IMS America.

NOTE: Generic market share is calculated as a percentage of all prescription drugs sold, not just off-patent drugs. These figures are based on countable units, such as tablets or capsules; prescription drugs that come in injectible form are not included.

46. CBO's 1996 paper on the Medicaid rebate program also found that the largest discounts were significantly higher for multiple-source drugs than for single-source drugs. In 1991, the largest discounts offered on multiple-source innovator drugs averaged 50 percent off the price to pharmacies, compared with 35 percent off for single-source drugs; see Congressional Budget Office, *How the Medicaid Rebate on Prescription Drugs Affects Pricing in the Pharmaceutical Industry*. See also Fiona Scott Morton, "The Strategic Response by Pharmaceutical Firms to the Medicaid Most-Favored-Customer Rules," *RAND Journal of Economics*, vol. 28, no. 2 (Summer 1997), pp. 269-290.

47. Those figures come from IMS America and are published in Pharmaceutical Research and Manufacturers of America, *1997 Industry Profile*, p. 40. The publication gave the generic market share in 1996 as 41.6 percent. The corrected 1996 figure came from a personal communication from Paul Wilson, Vice President of Statistical Services, IMS America, on February 27, 1998.

48. "Approximately 57 percent of all prescriptions paid for by managed care are still filled with branded products—a virtually identical ratio to the overall market," implying a generic market share of about 43 percent for the retail pharmacy market; see IMS America, "IMS Says Managed Care Drove Unprecedented Growth in Pharmaceuticals in 1996" (press release, April 14, 1997, available at http://www.ims-america.com/communications/pr_growth.html).

FDA approval before the patent on the innovator drug they were copying had expired. Those changes both increased the probability that a generic copy would become available after patent expiration and reduced the average delay between patent expiration and generic entry from more than three years to less than three months.

As generic drugs are substituted for their more expensive brand-name counterparts, the average price of a prescription falls. In CBO's retail pharmacy data set, the average retail prescription price for a brand-name drug with generic substitutes was $37 in 1994. However, including prescriptions that were filled with a generic drug, the average prescription price for a multiple-source drug was only $26. Thus, generic substitution lowered the average cost for a multiple-source prescription by $11. That result is only a rough estimate, however, since prescriptions may somewhat misrepresent the relative quantities of brand-name and generic drugs sold. For example, if generic drugs tend to have more pills dispensed per prescription than their brand-name counterparts, that estimate would understate the degree to which generic substitution reduces the average cost of a prescription. If generic drugs tend to have fewer pills dispensed, the reverse would be true.

Effect of Generic Entry on Sales

For many innovator drugs whose patents have recently expired, generic copies quickly gain a large share of the market. CBO's retail pharmacy data set includes 21 innovator drugs whose first generic competitors entered the market between 1991 and 1993. During the first full calendar year in which those 21 drugs faced generic competition, generics already accounted for an average of 44 percent of prescriptions dispensed through pharmacies.[49] Generics also cost one-fourth less than the brand-name drugs, on average, at retail prices. For seven of those drugs (Anaprox, Feldene, Lopid, Naprosyn, Pamelor, Tavist, and Xanax), generics had gained 65 percent or more of the innovator's market by 1994. For all but two of the 21 drugs, generic entry occurred within one year of patent expiration, and in many cases within three months.[50]

Other studies examining the size of the generic market after patent expiration have yielded slightly different results. Those appear to be attributable to differences in the sample of drugs studied as well as to small differences in method. A study by Grabowski and Vernon found that 11 drugs whose patents expired between 1989 and 1992 had an average generic market share (measured by quantity sold) of 50 percent in the first year after generic entry, and eight drugs whose patents expired in the 1986-1987 period had an average generic market share of 38 percent.[51] The study also found that the wholesale price of generic drugs was about half that of brand-name drugs in the first year after generic entry.

Grabowski and Vernon's average generic market share for the 1989-1992 period is higher than that measured by CBO for the 1991-1993 period in part because CBO included the quantity sold of all dosage forms of the brand-name drug, even those for which generic entry had not occurred, when calculating the percentage of total prescriptions filled with a generic drug. That method takes account of the option that brand-name manufacturers have to introduce a new dosage form (such as an extended-release capsule) just as a drug's patent is about to expire, so as to benefit from a three-year exclusivity period on that dosage form. Occasionally, manufacturers can even get a separate patent on a new dosage form. Of the 21 brand-name drugs that CBO analyzed, four had an advanced dosage form (Sinemet CR, Cardizem CD, Toprol XL, and Procardia XL) that was not yet available from generic manufacturers.

The Congress's former Office of Technology Assessment (OTA) also studied the erosion of brand-name drug sales after patent expiration.[52] In OTA's study of 35 brand-name drugs that lost patent protec-

49. The 44 percent average is weighted by sales revenues of the innovator drugs. The unweighted average is 42.8 percent.

50. The two drugs for which generic entry took more than a year after patent expiration had retail pharmacy sales of about $130 million in 1991.

51. Henry Grabowski and John Vernon, "Longer Patents for Increased Generic Competition in the U.S.: The Hatch-Waxman Act After One Decade," *PharmacoEconomics* (1996).

52. Office of Technology Assessment, *Pharmaceutical R&D*, Table F-3, p. 297.

tion between 1984 and 1987, sales volume for those drugs was 43 percent lower three years after patent expiration. Part of the reason it took that long for brand-name sales to erode by so much was a longer delay between patent expiration and generic entry during the period that OTA examined. For more than half of the 1984-1987 period, generic manufacturers could not have begun the abbreviated drug-approval process far enough in advance to enter the market soon after patent expiration. Also, that study differed from CBO's analysis because it focused on the decline in brand-name sales following patent expiration rather than explicitly on generic market share. Actual generic market share measured in volume may have been greater than 43 percent if the total quantity of the drugs demanded rose because generic drugs were cheaper. Or generic market share may have been smaller if competition from similar brand-name drugs was also eroding innovators' sales. OTA's estimates also differed from CBO's in that its measurements were based on the date of patent expiration rather than the date of generic entry.

Before 1984 and the Hatch-Waxman Act, competition from generic drugs in terms of price and market share was limited primarily to antibiotics.[53] In 29 cases other than antibiotics in which top-selling brand-name drugs had generic copies available, generic market share averaged just 12.7 percent of prescriptions dispensed through retail pharmacies in 1980.[54] The probability of generic entry was also much lower before 1984. Excluding antibiotics and drugs approved before 1962 (for which an abbreviated generic-drug-approval process existed), only 18 out of 52 top-selling drugs with expired patents had generic versions available.[55] Clearly, the lengthy FDA approval process at that time hampered the generic drug industry.

Effect of Generic Entry on Brand-Name Prices

Those consumers who are more sensitive to price, or who are covered by health plans that encourage generic substitution, are more likely to buy a generic drug when it becomes available. As the more price-sensitive consumers switch to the generic version, demand for the original brand-name drug declines and may become less sensitive to price. If that happens, the price of the brand-name drug could theoretically rise more quickly over time than it would have without generic competition.[56]

A number of empirical studies have found that the prices of brand-name drugs continue to rise faster than inflation after generic entry (see Box 4 for details). One study also found that brand-name prices increase by about 1 percent with each new generic competitor. At the same time, CBO's analysis shows that discounts on brand-name drugs tend to increase after generic entry, something not fully captured in the invoice prices on which the other empirical studies are based. CBO found that the best-price discount is 10 to 17 percentage points greater when two or more generic manufacturers produce copies of the brand-name drug (see Appendix B). Taken together, the implication of those results is that prices of brand-name drugs do rise faster than inflation for many final purchasers after generic entry, but some purchasers pay less for those drugs after generic entry.

CBO examined the prices that manufacturers charged for 34 brand-name drugs distributed to retail pharmacies that first saw generic competition after 1991. It found that those brand-name prices continued to increase faster than inflation after generic entry, perhaps as much as they would have otherwise.[57]

53. See Federal Trade Commission, Bureau of Consumer Protection, *Drug Product Selection* (1979), p. 46.

54. See Appendix C for details.

55. Those drugs were all in the top 200 drugs in the United States, rated by sales. Henry Grabowski and John Vernon, "Longer Patents for Lower Imitation Barriers: The 1984 Drug Act," *American Economic Review*, vol. 76, no. 2 (May 1986), pp. 195-198.

56. Frank and Salkever have developed a theoretical model that formally captures this phenomenon, showing that it may be profitable for the manufacturer of the innovator drug to raise its price after generic entry; see Richard G. Frank and David S. Salkever, "Pricing, Patent Loss and the Market for Pharmaceuticals," *Southern Economic Journal* (October 1992), pp. 165-179.

57. The analysis was based on the average price that manufacturers charged for brand-name drugs sold to the retail pharmacy class of trade, as reported by manufacturers to the Health Care Financing Administration as part of the Medicaid rebate program. Those prices, which include all discounts and rebates to retail pharmacies, were matched to the drugs in the retail pharmacy data set to determine whether a generic substitute existed. (For more details on the pricing data, see Appendix A.)

That result affects primarily third-party payers that do not manage their outpatient drug benefits and consumers who have no insurance (but who still purchased the brand-name drug). Other types of purchasers, such as Medicaid and PBMs, get rebates from manufacturers that are not captured in the prices charged to pharmacies.

For 34 drugs that experienced generic competition for the first time after 1991, the average price in-

Box 4.
Studies of How Generic Entry Affects Brand-Name Prices

Several economists have studied what happens to the prices of innovator drugs when generic copies enter the market. All of the studies agree that the effect on innovators' prices is very small, although there is some dispute about the direction of that effect. (Those studies looked at average invoice prices paid by hospitals and pharmacies, which do not include some types of discounts and rebates offered by drug manufacturers.)

For 18 innovator drugs whose patents expired between 1983 and 1987, Grabowski and Vernon found that prices continued to rise faster than inflation after generic entry.[1] Another empirical study, by Caves, Whinston, and Hurwitz, examined 30 brand-name drugs that went off patent between 1976 and 1987. The authors attempted to control for the rate of price increase that would have occurred without generic entry. They concluded that although the prices of many brand-name drugs continued to rise after generic entry, those prices were still lower than they would have been otherwise. The study's results showed that the brand-name price actually increased slightly just after patent expiration and then declined by only 2 percent with the entry of the first generic manufacturer.[2] After five generic manufacturers had entered the market, the brand-name price was 8.5 percent lower than it would have been without generic entry, and after 10 generic manufacturers had entered the market, that price was 15 percent lower.

Wiggins and Maness showed that generic entry has been effective in lowering the brand-name price for anti-infective drugs.[3] And a recent study by Ellison and colleagues found that in one antibiotic market (cephalosporins), demand for a brand-name drug is more sensitive to changes in the price of its generic substitute(s) than to changes in the price of a competing brand-name drug.[4] (Price competition between brand-name and generic drugs in the anti-infective class is thought to be unusually strong, however.)[5]

One study by Frank and Salkever of 32 drugs that went off patent between 1984 and 1987 found that brand-name prices increased more quickly than if generic entry had not occurred—by approximately one extra percentage point for each generic entrant.[6]

Overall, brand-name prices frequently continue to rise after generic entry. Whether they rise more quickly or more slowly than would be the case without competition from generic drugs, however, is unclear based on these studies.

1. Henry Grabowski and John Vernon, "Brand Loyalty, Entry, and Price Competition in Pharmaceuticals After the 1984 Drug Act," *Journal of Law and Economics* (October 1992), p. 339.

2. Generic entry occurs much sooner after patent expiration now than during most of the period studied by the authors, because of changes made by the Hatch-Waxman Act. Richard E. Caves, Michael D. Whinston, and Mark A. Hurwitz, "Patent Expiration, Entry, and Competition in the U.S. Pharmaceutical Industry," *Brookings Papers on Economic Activity: Microeconomics* (1991), pp. 1-66.

3. Steven Wiggins and Robert Maness, "Price Competition in Pharmaceuticals: The Case of Antiinfectives" (draft, Texas A&M University, Department of Economics, 1995).

4. Sara Fisher Ellison and others, "Characteristics of Demand for Pharmaceutical Products: An Examination of Four Cephalosporins," *RAND Journal of Economics*, vol. 28, no. 3 (Autumn 1997), pp. 426-446.

5. Office of Technology Assessment, *Pharmaceutical R&D: Costs, Risks and Rewards* (February 1993); and Grabowski and Vernon, "Brand Loyalty, Entry, and Price Competition," p. 333. Antibiotics are also known as a class for which physicians are more likely to write the prescription in generic form (specifying a chemical name) than with a brand name.

6. Richard G. Frank and David S. Salkever, "Generic Entry and the Pricing of Pharmaceuticals," *Journal of Economics and Management Strategy*, vol. 6 (Spring 1997), pp. 75-90.

crease between 1991 and 1994 was 22 percent. By comparison, average prices for brand-name drugs that faced no generic competition rose by 24.5 percent over that period. And the prices of brand-name drugs that had already faced generic competition by 1991 grew by 22.4 percent during the same period. (Apart from any effect of generic competition, that price increase for multiple-source drugs could be lower because many of the drugs are older ones that have been surpassed by newer treatments.) The differences in the rate of price increase among those three groups of brand-name drugs are small and consistent with the notion that generic competition does not have a large effect on brand-name prices for many purchasers.

Effect of Generic Competition on Total Costs for Prescription Drugs

Because generic drugs are priced much lower than their brand-name counterparts, they are a source of substantial savings. According to CBO's data on retail pharmacy sales, the average retail price of a prescription for a generic drug in 1994 was $17.40 (see Table 1 on page 15). Multiple-source brand-name drugs were twice as expensive—averaging $37.40 per prescription.

CBO estimates that if each generic prescription had been dispensed at the corresponding brand-name price, purchasers of prescription drugs through retail pharmacies would have spent roughly $8 billion to $10 billion more in 1994. Those figures were calculated as follows: CBO assumed that all of the generic prescriptions dispensed in 1994 would have been filled with a higher-priced brand-name drug if the generic drug was not available.[58] Then the price difference between the innovator and generic formulations of a given drug was multiplied by the number of generic prescriptions dispensed for that drug. Adding together the results of those calculations for all of the multiple-source drugs in the retail pharmacy data set yielded an estimate of $7 billion in direct savings from retail purchases of generic drugs in the data set.[59]

The sales data cover only 70 percent of the retail pharmacy market, however, although they may cover more than 70 percent of generic drug sales through retail pharmacies since they include nearly all of the 200 top-selling drugs that are dispensed primarily through pharmacies. Assuming that the data set encompasses 70 percent to 90 percent of total generic sales, then savings from all retail purchases of generic drugs through pharmacies would total approximately $8 billion to $10 billion in 1994. Of course, retail pharmacies are not the only sellers of prescription drugs. Since other channels (including hospitals, clinics, and mail-order pharmacies) distribute around 40 percent of prescription drugs, the total savings from generic substitution through all channels were most likely even greater than that amount.

That calculation entails a variety of assumptions and caveats. First, it assumes that the quantity of prescriptions filled for a particular multiple-source drug does not increase because a lower-priced generic has become available. If the number of prescriptions did increase, the calculation would overstate the savings from generic entry. However, limited statistical evidence supports the assumption that the quantity sold does not change. A study by Caves, Whinston, and Hurwitz found that the total amount sold of a drug in both generic and brand-name forms did not increase after generic entry.[60]

Second, the calculation is a rough one because the price per prescription, from which it is derived, does not account for possible systematic differences between the size of brand-name and generic prescriptions. The calculation would be more accurate—though much more cumbersome—if the unit of measure was the cost of an average daily dose. But even

58. Technically, the calculation assumed that demand is perfectly price inelastic—that is, the lower price of generic drugs does not induce more prescriptions to be filled than if the cheaper generic version did not exist. To the extent that people fill prescriptions they would have left unfilled if a cheap generic version was not available, the estimate somewhat overstates the savings from generic substitution. And to the extent that some consumers substitute the generic for a therapeutically similar (but chemically different) brand-name drug that is still under patent, savings from generic substitution exist but the calculation estimates them based on the wrong brand-name price. That may or may not lead to a small overstatement of the total savings.

59. Those savings were calculated only for tablet and capsule dosage forms, which constitute 91 percent of the value of generic sales in the retail pharmacy data set. Those dosage forms yield a more reliable average price per prescription, which forms the basis of the calculation.

60. Caves, Whinston, and Hurwitz, "Patent Expiration, Entry, and Competition in the U.S. Pharmaceutical Industry."

that measure contains problems, because the average daily dose can vary among people and among the different medical conditions that a drug is used for. Without the ability to use a better measure, the calculation relies on prescriptions as the unit of quantity to obtain a rough estimate of the savings from generic substitution.

Finally, the calculation does not include any rebates that manufacturers pay to PBMs or other purchasers of prescription drugs through retail pharmacies. Excluding those rebates leads to an overestimation of the savings from generic substitution at retail pharmacies. That overestimate could be as much as roughly $500 million, assuming that manufacturers give rebates on multiple-source brand-name drugs (to PBMs and other third-party payers that manage their outpatient drug benefits) to the same extent that they do on brand-name drugs still under patent.[61]

Competition Among Generic Drugs

The expiration of an innovator drug's patent frequently prompts more than one generic copy to enter the market. Since most generic competitors sell their copy under the same chemical name, there is little apparent difference between their products. Economic theory suggests that differences between products dampen price competition, so when products are roughly identical, price competition can be intense. Hence, as more generic manufacturers enter the market, they should face increased pressure to lower prices in order to maintain market share.

Tabulations of average retail prescription prices in 1994 show that the average price of a generic drug does decline as the number of manufacturers and distributors of that drug increases (see Table 5). For example, the average prescription price of a generic drug with one to five manufacturers ($23.40) is more than that of a drug with 16 to 20 manufacturers ($19.90). CBO's retail pharmacy data set covers 112 innovator drugs that in 1994 were also available in generic forms sold under their chemical name. Comparing the average generic prescription price with the average innovator price for the same drug also shows prices falling as the number of generic manufacturers rises. When one to 10 generic manufacturers are in the market, the generic retail prescription price averages 61 percent of the brand-name price. When 11 to 24 generic manufacturers are in the market, the generic retail price averages less than half of the brand-name price.

Other studies have also concluded that prices of generic drugs decline in response to increased generic competition. Economist Richard Caves and colleagues found that as the number of generic manufacturers increased from one to 10, the average generic price fell from 60 percent to just 34 percent of the brand-name price. With 20 manufacturers, the generic price was only 20 percent of the brand-name price.[62] Since generic prices tend to fall as the number of producers rises, generic manufacturers are most profitable when they are one of the first to enter a market.

Market Concentration in the Generic Drug Industry

Overall, the generic drug market is not particularly concentrated. Mylan and Geneva, the largest generic firms in 1994, accounted for 16 percent and 12 percent, respectively, of all generic sales in the retail pharmacy data set. Most generic firms had just 1 percent to 5 percent of total generic sales.

61. Discounts and rebates to private purchasers in 1994 totaled $3,456 million (not including Medicaid rebates), according to information that the Pharmaceutical Research and Manufacturers of America provided to CBO on April 28, 1997. Pharmacies distribute 60 percent of prescription drugs, but only rebates to third-party payers, not the discounts to pharmacies themselves, should be counted. Assuming that 40 percent of the discounts and rebates went to PBMs and other purchasers that manage their outpatient drug benefits (a very generous amount), that leaves $1,382 million. Since multiple-source brand-name drugs represent about 33 percent of the value of all brand-name drugs sold through retail pharmacies, taking 33 percent of that leaves $455 million.

62. Caves, Whinston, and Hurwitz, "Patent Expiration, Entry, and Competition in the U.S. Pharmaceutical Industry," p. 36, Table 9. Their study actually counted the number of approved abbreviated new drug applications, which a generic manufacturer is required to obtain from the FDA, rather than the number of manufacturers and distributors.

Table 5.
Price Comparison of Generic and Innovator Drugs, by Number of Manufacturers, 1994

Number of Manufacturers Selling Generic Copies of a Given Innovator Drug[a]	Number of Innovator Drugs in Category	Average Prescription Price of All Generic Drugs in Category (Dollars)	Average Prescription Price of All Innovator Drugs in Category (Dollars)	Average Ratio of the Generic Price to the Innovator Price for the Same Drug[b]
1 to 5	34	23.40	37.20	0.61
6 to 10	26	26.40	42.60	0.61
11 to 15	29	20.90	50.20	0.42
16 to 20	19	19.90	45.00	0.46
21 to 24	4	11.50	33.90	0.39
Average	n.a.	22.40	43.00	0.53

SOURCE: Congressional Budget Office based on tabulations of retail pharmacy sales data from Scott-Levin.

NOTES: The retail pharmacy data covered 177 multiple-source drugs, but only 112 had both brand-name and generic versions and came in tablet or capsule form. Only tablet and capsule formulations were used for calculating average prescription prices. The average number of generic manufacturers and distributors for a given drug was 10. Only manufacturers with sales above $100,000 for at least one dosage form were counted in the groupings, although all generic sales were used to calculate the average generic price.

n.a. = not applicable.

a. Includes manufacturers and distributors of dosage forms with annual sales above $100,000.

b. An unweighted average of the ratios of generic to brand-name retail pharmacy prices for the drugs in each category. The ratio for a multiple-source drug is equal to: (total generic sales/number of generic prescriptions) ÷ (total brand-name sales/number of brand-name prescriptions).

The markets for individual multiple-source drugs, by contrast, are much more concentrated. For 94 of 110 multiple-source drugs in the retail pharmacy data set, the top two generic firms were responsible for more than half of generic sales. And for 57 of those drugs, the single top generic firm accounted for more than half of generic sales.

Leading generic firms may lower their price when new competitors enter the market so as to maintain their dominant position. That would explain how the average generic price falls as the number of manufacturers rises, but sales of many generic drugs remain dominated by one or two companies. Still, Grabowski and Vernon found that in only half of the 18 markets they examined, the lowest-priced generic manufacturer had the largest market share.[63] Factors other than price, such as being the first to enter a market, probably also play a role in determining a generic manufacturer's market share. And one recent study found that generic manufacturers are more likely to enter markets where they have some experience with a drug's dosage form, therapy, or active ingredient.[64]

Links Between Generic and Brand-Name Manufacturers

Although the same company rarely produces both a brand-name drug and its generic copy, some generic manufacturers are subsidiaries of brand-name firms. In 1994, eight of the 15 largest generic companies in

63. Henry Grabowski and John Vernon, "Brand Loyalty, Entry, and Price Competition in Pharmaceuticals After the 1984 Drug Act," *Journal of Law and Economics* (October 1992), p. 345. CBO's retail pharmacy data are in retail prices, so they cannot be used to compare the prices charged by different generic manufacturers.

64. Fiona Scott Morton, *Entry Decisions in the Generic Pharmaceutical Industry*, Working Paper No. 6190 (Cambridge, Mass.: National Bureau of Economic Research, September 1997).

the retail pharmacy data set were owned by innovator firms.[65] Those generic subsidiaries were responsible for 46 percent of total generic sales in the data set.

Today, the proportion of generic drugs produced by subsidiaries of innovator firms is probably somewhat smaller than in 1994 because several brand-name manufacturers have left the generic drug business. For example, three of the eight larger generic firms owned by a brand-name company (Rugby, Hamilton, and Warner-Chilcott) have been sold or disbanded in recent years.[66] Some of those brand-name companies experimented with producing generic copies of their own drugs in the early 1990s and found that it was not very profitable. For example, generic manufacturer Hamilton offered copies of the brand-name drugs Anaprox and Naprosyn produced by its parent company, Syntex. During the first calendar year after patent expiration, the average generic price quickly dropped, and Syntex lost 70 percent of its market for those two drugs to generic competition.[67] A few of the brand-name companies that tried to get further into the generic business in the early 1990s, including Hoechst Marion Roussel and Merck, have recently sold generic subsidiaries.[68]

Nevertheless, brand-name companies that have long held generic subsidiaries remain committed to their generic business. Today, at least 13 manufacturers of innovator drugs have a generic subsidiary or division (see Table 6). One of the largest generic firms, Geneva Pharmaceuticals, is a subsidiary of Novartis (a company formed by the merger of Ciba-Geigy and Sandoz).

Most generic subsidiaries do not produce copies of their parent company's drugs. Out of 112 multiple-source drugs in the retail pharmacy data set, only 13 had a generic subsidiary of the brand-name manufacturer selling more than 10 percent of the prescriptions dispensed through retail pharmacies. In general, the incentives to lower price in order to gain market share are the same for all generic manufacturers, whether or not they are the subsidiary of an innovator firm. But an important exception occurs when the generic subsidiary produces a copy of the parent company's innovator drug. Though infrequent, in such cases the subsidiary may have less incentive to lower price than other generic producers because it does not want to take more sales away from the parent company's drug. And when the generic subsidiary does lower price dramatically, the innovator firm suffers.

Table 6.
Generic Subsidiaries or Divisions of Brand-Name Manufacturers

Generic Manufacturer	Owned By
Apothecon	Bristol-Myers Squibb Co.
Arcola Laboratories	Rhone-Poulenc Rorer
Blue Ridge Laboratories	Marion Merrell Dow Inc.
Copley Pharmaceutical Inc.	Hoechst Marion Roussel
Dista Products Co.	Eli Lilly and Co.
Elkins-Sinn Inc.	American Home Products Corp.
ESI-Lederle	American Home Products Corp.
Geneva Pharmaceuticals	Novartis Corp.
Greenstone Ltd.	Pharmacia & Upjohn Inc.
IPR Pharmaceuticals Inc.	Zeneca Pharmaceuticals
Kanetta Pharmacal	Sanofi Winthrop Inc.
Lederle Laboratories	Lederle Standard Products
Penn Labs Inc.	SmithKline Beecham
Schein Pharmaceutical Inc.	Bayer Corp.

SOURCES: "Generics Are Gaining Respect," *Med Ad News* (November 1993), p. 10; and "The Meltdown: A Special Report on the Generic Drug Industry," *Med Ad News* (November 1997), p. 31.

Conclusions

Changes to the approval process for generic drugs made by the Hatch-Waxman Act, combined with the changes in demand for generic drugs discussed in

65. All 15 companies had annual sales of over $100 million for the drugs in the retail pharmacy data set in 1994.

66. Rugby, which was owned by Hoechst Marion Roussel, was sold to Watson, a generic drug company. Hamilton, a subsidiary of Syntex, was disbanded when Syntex was acquired by Roche in 1995. And Warner-Chilcott was sold by Warner-Lambert to Nalé Laboratories.

67. Based on CBO's retail pharmacy data set. Also see Catherine Yang, "The Drugmakers vs. the Trustbusters," *Business Week*, September 5, 1994, p. 67.

68. Milt Freudenheim, "Cleaning Out the Medicine Cabinet," *New York Times*, September 11, 1997, p. D1. Hoechst Marion Roussel sold Rugby in 1997 but still owns two smaller generic subsidiaries.

Chapter 2, have prompted a dramatic rise in generic competition since 1984. That increased competition has helped hold down the average price of a multiple-source prescription drug by encouraging the substitution of lower-priced generic drugs for brand-name ones. In 1994, such substitution saved final purchasers of prescription drugs through retail pharmacies roughly $8 billion to $10 billion (at retail prices).

Manufacturers of generic drugs, who sell nearly identical versions of the same product, compete more intensely on the basis of price than do manufacturers of innovator drugs, who compete more on the basis of quality and other differences between products. Average list and invoice prices of brand-name drugs do not typically fall after generic competitors enter the market. On a selective basis, however, manufacturers of brand-name drugs do offer discounts and rebates to some purchasers, and those discounts tend to be larger when generic versions of the drug are available. The data necessary to determine what volume of purchases is sold at a substantial discount do not exist. The industry group Pharmaceutical Research and Manufacturers of America estimates that discounts saved purchasers $5.3 billion in 1994, $3.5 billion of which went to non-Medicaid purchasers.[69] (That $3.5 billion represented over 5 percent of the value of non-Medicaid prescription drug sales.)

The extent to which brand-name drugs compete through price is difficult to assess. Limited empirical evidence suggests that competition between similar brand-name drugs causes their prices to rise more slowly over time than would otherwise be the case. However, evidence also suggests that the prices of me-too drugs increase much more rapidly over time than the price of the breakthrough drug. Much of that analysis is based on list prices or average invoice prices, which do not include many charge-backs and rebates.

Clearly, some price competition is occurring, particularly in the segment of the market that can negotiate discounts when several similar brand-name drugs are available. As Chapter 2 noted, that segment of the market is growing with the emergence of PBMs and the proliferation of other managed care techniques. Still, since the size of discounts and the quantity of drugs sold at a discount are not known, it is difficult to assess the extent of competition brought about through discounting.

69. The group's $5.3 billion estimate is based on reporting from its member companies. In 1994, manufacturers paid states $1.8 billion under the Medicaid rebate program, leaving a net value of $3.5 billion in discounts to non-Medicaid purchasers.

Chapter Four

The Effects of the Hatch-Waxman Act on the Returns from Innovation

The Hatch-Waxman Act helped increase the supply of generic drugs by lowering the cost of getting them approved by the Food and Drug Administration. As a result of that act and structural changes in the demand for prescription drugs, more innovator drugs now face generic competition shortly after their patents expire. They then quickly lose over 40 percent of their market, on average, to generic drugs.

By themselves, the increase in generic market share and the acceleration of generic entry after patent expiration would have substantially reduced the returns from marketing an innovator drug. However, the Hatch-Waxman Act countered part of that effect by providing patent extensions for such drugs, which now average about three years. Those patent extensions offset part of the potential loss. But they do not completely protect the returns of brand-name manufacturers from the dramatic rise in market share for generic drugs.

The analysis in this chapter focuses on changes in patent protection for brand-name drugs as well as on supply-side factors that have boosted generic market share. As noted in Chapter 2, however, demand-side factors, such as the rise of managed care techniques, have also played a role. The Congressional Budget Office's estimate of changes in the returns from marketing a new drug takes those demand-side factors into account only through their contribution to the dramatic growth of generic market share since 1984.

The Hatch-Waxman Act has increased the likelihood that generic copies will become available once the patent on a brand-name drug expires. Before the act (in 1983), only 35 percent of the top-selling drugs no longer under patent had generic copies available.[1] Today, nearly all do.[2] At the same time, the share of their market that those drugs lose to generic competitors has also expanded dramatically. In 1980, generic drugs accounted for only around 13 percent of the total quantity of prescriptions sold for multiple-source drugs (excluding antibiotics).[3] Fourteen years later, they constituted 58 percent of the total quantity of multiple-source prescriptions dispensed (according to CBO's retail pharmacy data set). Pinpointing how much of that increase resulted solely from the Hatch-Waxman Act, however, is impossible.

For the minority of brand-name drugs that would have experienced generic competition even without the

1. That figure is based on the top 200 off-patent drugs that year, excluding antibiotics and drugs that were approved before 1962; see Henry Grabowski and John Vernon, "Longer Patents for Lower Imitation Barriers: The 1984 Drug Act," *American Economic Review*, vol. 76, no. 2 (May 1986), pp. 195-198.

2. For example, in 1994, 95 percent of the off-patent drugs with sales revenues of $40 million or more in CBO's retail pharmacy data set had generic copies available. In that case, off-patent drugs were ones that were not protected by a patent or an exclusivity provision.

3. CBO calculated that average based on 29 nonantibiotic multiple-source drugs that were among the top 100 in U.S. sales, using data from Alison Masson and Robert Steiner, *Generic Substitution and Prescription Drug Prices: Economic Effects of State Drug Product Selection Laws* (Federal Trade Commission, October 1985), pp. 251-269. See Appendix C of this study for details.

act, the average number of years they are on the market before facing generic competition did not change much. Before 1984, an average of three years elapsed between patent expiration and generic entry. By accelerating the approval process for generic drugs and explicitly permitting them to undergo clinical tests while the innovator drug is still under patent, the Hatch-Waxman Act now enables generic manufacturers to enter a market almost immediately after patent expiration. However, that decline of roughly three years in the average time before generic entry is almost exactly offset by the average increase in patent terms from Hatch-Waxman extensions.

CBO's analysis finds that despite the patent-term extensions and various exclusivity provisions of the Hatch-Waxman Act, the increase in generic market share since 1984 has decreased the total returns from marketing a new drug by about $27 million, on average. (That estimate does not apply to antibiotic drugs, which were not affected by the act.) In this study, the phrase "returns from marketing a new drug" refers to the expected average present discounted value of the total profit stream generated by introducing a new drug onto the market. Previous studies estimated that profit stream at an average of $210 million to $230 million (in 1990 dollars) for drugs introduced in the early 1980s.[4] Those returns account for production costs but not the cost of research and development, which averaged about $200 million per drug (in 1990 dollars) when capitalized to the date of market introduction. Expressed as a percentage, the $27 million decline in returns equals roughly 12 percent of the total average returns from marketing a new drug. Despite that decline, those expected returns probably continue to cover the costs of developing a drug, on average, including the cost of capital.[5]

Changes to the Length of Patents for Brand-Name Drugs

Over the past 14 years, federal legislation—particularly the Hatch-Waxman Act of 1984 and the Uruguay Round Agreements Act of 1994—has altered the patent protection available to pharmaceutical products in the United States (see Table 7). The average length of time between when a brand-name drug enters the market and when its patent expires rose by more than two years—from an average of about nine years before 1984 to 11 to 12 years.[6] By contrast, the period after that, between when the innovator drug's patent expires and when the first generic copy enters the market, declined from about three years to a few months. After patent expiration, sales of an innovator drug can decline significantly. Between 1984 and 1994, the average market share of generic drugs increased from around 13 percent to 58 percent of prescriptions dispensed for multiple-source drugs (except antibiotics).[7]

Determining the extent to which average patent terms have changed under the Hatch-Waxman Act is crucial to assessing whether the returns from marketing a new drug have largely been preserved despite the dramatic rise in generic competition. To that end, CBO analyzed data from the Patent and Trademark Office to evaluate the effect of Hatch-Waxman extensions on the average patent term of an innovator drug.

4. See Office of Technology Assessment, *Pharmaceutical R&D: Costs, Risks and Rewards* (February 1993); and Henry G. Grabowksi and John M. Vernon, "Returns to R&D on New Drug Introductions in the 1980s," *Journal of Health Economics*, vol. 13, no. 4 (December 1994), pp. 383-406.

5. Ibid. Those two studies found that the present discounted value of the returns from marketing a drug exceeded the capitalized costs of drug development by an average of $22 million to $36 million for drugs introduced in the early 1980s.

6. According to data that CBO obtained from the Patent and Trademark Office, the average patent term remaining after FDA approval was 11.5 years for the 51 drugs approved between 1992 and 1995 that received a Hatch-Waxman extension. For drugs approved between 1978 and 1982, the average patent term remaining was just over nine years, according to Office of Technology Assessment, *Pharmaceutical R&D*, p. 83.

7. According to CBO's retail pharmacy data set, generic drugs accounted for 36 percent of all retail prescriptions dispensed in 1994 and 58 percent of prescriptions dispensed for multiple-source drugs. Excluding the few multiple-source antibiotic drugs from the data does not particularly affect that average.

Table 7.
Changes in Patent Protection for U.S. Pharmaceuticals

	Before the Hatch-Waxman Act of 1984	After the Hatch-Waxman Act and the Uruguay Round Agreements Act of 1994
Patent Term	17 years from patent grant	20 years from application filing (the earliest relevant filing date)[a]
Average Period of Marketing Under Patent Protection[b]	About 9 years	About 11.5 years
Usual Period Between Patent Expiration and Generic Entry[c]	3 to 4 years	Frequently 1 to 3 months
Average Generic Market Share for Multiple-Source Drugs (Percent)[d]	12.7	57.6

SOURCE: Congressional Budget Office based in part on the sources in the footnotes below.

NOTE: These figures exclude antibiotics, which were not affected by the Hatch-Waxman Act.

a. See 35 U.S.C. 154(c)(1). For drugs patented before June 8, 1995, companies can choose between the 17-years-from-patent term and the 20-years-from-filing term (if the drug was not yet into its Hatch-Waxman extension on that date).

b. The average "effective" patent term (the period between approval by the Food and Drug Administration and patent expiration). These averages differ from the sales-weighted averages used in calculating the returns from marketing a new drug. Top-selling drugs tend to have more years of marketing under patent protection, making the sales-weighted averages larger. The figure for the pre-Hatch-Waxman period is based on Office of Technology Assessment, *Pharmaceutical R&D: Costs, Risks and Rewards* (February 1993); and Henry Grabowski and John Vernon, "Longer Patents for Lower Imitation Barriers: The 1984 Drug Act," *American Economic Review*, vol. 76, no. 2 (May 1986). The figure for the post-Hatch-Waxman period is based on the average effective patent term for the 51 drugs approved between 1992 and 1995 that received a Hatch-Waxman extension.

c. The pre-Hatch-Waxman figure is based on CBO's analysis of generic entry for 11 nonantibiotic drugs approved after 1962. The post-Hatch-Waxman figure is based in part on Henry Grabowski and John Vernon, "Longer Patents for Increased Generic Competition in the U.S.: The Hatch-Waxman Act After One Decade," *PharmacoEconomics* (1996).

d. The increase resulted from various changes in the structure of demand for brand-name and generic drugs as well as from changes in the Hatch-Waxman Act. The pre-Hatch-Waxman figure is based on sales data for 29 multiple-source drugs (excluding antibiotics) in Table A5-1 of Alison Masson and Robert Steiner, *Generic Substitution and Prescription Drug Prices: Economic Effects of State Drug Product Selection Laws* (Federal Trade Commission, October 1985).

Patent Extensions Under the Hatch-Waxman Act

The Hatch-Waxman Act allows for patent extensions based on the amount of time a drug spends in the FDA review process. Those extensions now average about three years for new drugs.[8] Technically, the length of a patent extension equals half of the time spent in clinical testing after the patent is granted, plus all of the time that the FDA spends reviewing the new drug application. (The clinical testing phase starts when the manufacturer files an investigational new drug application, which allows clinical testing in humans to take place.) Those extensions are subject to two limits.

8. The average extension for drugs approved before 1992 was less than that because a transitional two-year cap applied to drugs that were in clinical testing when the Hatch-Waxman Act became law. Drugs whose clinical testing began before September 24, 1984, were limited to two years of patent extension, and drugs that were already on the market by that date were not eligible for any patent extensions. However, drugs approved between January 1, 1982, and September 23, 1984, were eligible for 10 years of market exclusivity before an abbreviated new drug application could be submitted to the FDA by a generic manufacturer.

Table 8.
Average Length of Hatch-Waxman Extensions for Drugs Approved Between 1992 and 1995

Year of FDA Approval	Number of New Drugs Receiving Extensions	Average Extension (Years)	
		For All Drugs	Excluding Drugs Subject to Two-Year Cap
1992	16	2.4	2.5
1993	14	3.2	3.4
1994	10	2.5	2.7
1995	11	3.6	3.6
Average	n.a.	2.9	3.0

SOURCE: Congressional Budget Office calculations based on data from the Patent and Trademark Office and the Food and Drug Administration.

NOTE: FDA = Food and Drug Administration; n.a. = not applicable.

First, they cannot exceed five years. And second, they cannot allow the period between product approval and patent expiration to exceed 14 years.

Only one patent for each newly approved chemical entity is eligible for a Hatch-Waxman extension. If a drug has more than one patent, the manufacturer must choose which will receive the extension. Extensions are usually applied to the patent on a drug's chemical compound (a product patent) or occasionally to a patent on the use of the drug.[9] Manufacturers must apply for an extension no more than 60 days after the FDA approves a drug for marketing.

For the 51 drugs approved between 1992 and 1995 that have received an extension, the average extension lasted 2.9 years. However, eight of those drugs were subject to a transitional two-year cap because they were undergoing clinical testing when the Hatch-Waxman Act became law. For the 43 drugs not subject to that cap, the average extension lasted 3.0 years (see Table 8).[10] In all, the average patent term remaining after FDA approval for the 51 drugs that received extensions was 11.5 years.

Given the length of the clinical testing and NDA approval phases, those extensions would have averaged more than three years were it not for the 14-year cap. A study of the first 65 drugs to receive Hatch-Waxman extensions found that the total extension available under the act's formula, before applying the caps and other restrictions, averaged 4.5 years.[11] Almost half of those drugs would have been subject to the 14-year cap had the transitional two-year cap not applied. Similarly, about half of the 43 drugs introduced between 1992 and 1995 that received Hatch-Waxman extensions and were not limited by the transitional cap had their extensions limited by the 14-year cap (see Table 9). Only 10 drugs had their extensions limited by the five-year cap.

9. A third type of patent, called a process patent, also exists. Since it may not be difficult to formulate a similar compound using a slightly different chemical process, those types of patents do not necessarily prevent generic entry; personal communication by Peter Richardson, chief patent attorney, Pfizer, May 1997.

10. A study by Henry Grabowski and John Vernon found that for about 70 innovator drug products whose patents expired between 1991 and 1993, Hatch-Waxman extensions averaged 2.4 years. Some of those drugs were subject to the transitional two-year cap. See Grabowski and Vernon, "Longer Patents for Increased Generic Competition in the U.S.: The Hatch-Waxman Act After One Decade," *PharmacoEconomics* (1996).

11. The average clinical testing period for those drugs lasted 5.1 years. After subtracting the time between the beginning of clinical tests and the issuing of the patent, that period came to 3.8 years, half of which is counted when calculating the extension. The average NDA approval phase for those 65 drugs was 2.6 years, for a total average potential extension of 4.5 years. See Alan D. Lourie, "A Review of Recent Patent Term Data," *Journal of the Patent and Trademark Office Society* (February 1989), pp. 171-176.

Not all drugs obtain a Hatch-Waxman extension. The FDA approved a total of 101 drugs containing new chemical compounds between 1992 and 1995, but only half (51) have received a Hatch-Waxman extension so far. Another 12 have an application pending (see Table 10). Of the remaining 38 drugs, 19 had no patent to extend. Fifteen others already had 14 years left under patent when they were approved by the FDA. And four drugs did not apply for an extension, for reasons that could not be determined.

Nonpatent Exclusivity Periods Under the Hatch-Waxman Act

In addition to extending patent terms, the act grants special periods of exclusivity in two circumstances (not including some of its transitional features). First, when the FDA approves a new chemical entity, no application for a generic copy is accepted for a minimum of five years. That provision benefits drugs that have no patent, or have a very short remaining patent life when they are approved, because it means that generic manufacturers must wait five years before filing an abbreviated new drug application. Since the approval process for such applications takes more than 30 months, on average, many of those brand-name drugs should actually have six to seven years of exclusivity before they must face generic competition.[12] In most cases, however, that period is probably too short to fully recover the average costs of drug development.

Table 9.
Limits on Hatch-Waxman Extensions for Drugs Approved Between 1992 and 1995

Type of Limit	Number of Drugs Affected
14-Year Cap	21
Five-Year Cap	10
Two-Year Cap	8
No Cap	12
Total	51

SOURCE: Congressional Budget Office based on data from the Patent and Trademark Office.

Table 10.
Reasons That Some Drugs Approved Between 1992 and 1995 Did Not Receive a Hatch-Waxman Extension

Reason	Number of New Drugs
No Patent to Extend[a]	19
Already Had 14 Years of Exclusivity	15
Extension Application Pending	12
Eligible but Did Not Apply	4
Total	50

SOURCE: Congressional Budget Office calculations based on data from the Patent and Trademark Office and from Department of Health and Human Services, Food and Drug Administration, "Prescription and OTC Drug Product Patent and Exclusivity Data," in *Approved Drug Products with Therapeutic Equivalence Evaluations* (1996).

NOTE: The Food and Drug Administration approved a total of 101 new drugs during this period.

a. These drugs received five years of exclusivity under the Hatch-Waxman Act or seven years of exclusivity under the Orphan Drug Act.

Second, the act allows the FDA to grant three years of market exclusivity for an NDA (including a supplemental one) if that application requires new clinical investigations. Manufacturers can use NDAs or supplemental NDAs to obtain approval for new dosage forms of an already-approved drug, for a new use, or for marketing the drug over the counter. Those provisions give manufacturers an incentive to continue improving brand-name drugs, and the knowledge about those drugs, after they are on the market.

Manufacturers can also use those provisions to slow generic competition. By introducing a new dos-

12. In 1995 and 1996, an average of 33 to 34 months elapsed between the submission and final approval of abbreviated NDAs; see Department of Health and Human Services, Food and Drug Administration, *Justification of Estimates for Appropriations Committees* (1997 and 1998).

age form just before patent expiration, a manufacturer obtains three years of market exclusivity for the new product under the Hatch-Waxman Act (although generic manufacturers can still copy the original form of the drug). Likewise, if a drug starts being sold over the counter, it enjoys three years of exclusivity before the FDA can accept abbreviated applications for generic over-the-counter versions. The over-the-counter versions of Zantac and Tagamet, for example, have benefitted from that provision. Sometimes, a manufacturer can obtain a separate patent on a new dosage form—particularly an extended-release form. For example, the patent for the active ingredient in Procardia expired in 1991, but the patents for the extended-release version, Procardia XL, do not expire until 2000 or later.[13]

The Effect of Those Changes on the Average Drug

To assess the change in returns from marketing a new drug, analysts need to know the average effect of the Hatch-Waxman Act on all brand-name drugs approved, not just on those that obtain an extension. When the benefits of the act's patent extensions and five-year exclusivity period are averaged over all drugs approved between 1992 and 1995, the average effect is to postpone generic entry by 2.8 years.

CBO calculated that effect as follows. As Table 8 shows, extensions averaged three years for the 43 drugs receiving a Hatch-Waxman extension during that period that were not subject to the transitional two-year cap. Since the transitional cap applies only to drugs in clinical testing in 1984, it will eventually disappear. Therefore, the calculation attributes three years of patent exclusivity to all 51 drugs that received a Hatch-Waxman extension. It also assumes that the 12 drugs with extension applications pending will receive an average extension of three years.

Of the 19 drugs that had no patent to extend, nine were excluded from the calculation because they were "orphan" drugs (those with a potentially small market because of the medical condition they treat), which received seven years of exclusivity under the Orphan Drug Act. The other 10 unpatented drugs were entitled under the Hatch-Waxman Act to five years of exclusivity, during which no generic manufacturer could file an abbreviated application with the FDA. Since it takes at least one year for a generic manufacturer to obtain FDA approval, that exclusivity provision effectively postpones generic entry by at least six years. Thus, the calculation attributes six years of delay in generic entry for those drugs under the act.

The average was taken over the number of new drugs approved between 1992 and 1995, after subtracting the nine orphan drugs and the four drugs that did not apply for an extension but were eligible. Mathematically, the formula is:

$$\frac{(\text{number of drugs obtaining an extension} \times 3 \text{ years}) + (\text{unpatented drugs} \times 6 \text{ years})}{(\text{all new drugs approved}) - (\text{orphan drugs}) - (\text{drugs that were eligible for an extension but did not apply})}$$

$$= [(51 + 12) \times 3 + (10 \times 6)]/(101 - 9 - 4) = 2.8.$$

That average does not take into account the exclusivity periods for new dosage forms. As explained below, CBO accounted for those exclusivity periods in its calculation of returns from marketing by including dosage forms that have no generic versions available in its estimate of average generic market share following patent expiration.

The Effect of the Uruguay Round Agreements Act

Ten years after the Hatch-Waxman Act, another piece of legislation, the Uruguay Round Agreements Act of 1994 (URAA), affected patent terms for brand-name drugs. That act changed the length of U.S. patents on all types of inventions to 20 years from the date of application rather than 17 years from the date the patent is granted. That change has had only a very small effect on the average "effective" patent term—the time between FDA approval and patent expiration—for drugs patented after June 8, 1995 (most of which have

13. Department of Health and Human Services, Food and Drug Administration, "Approved Drug Products with Therapeutic Equivalence Evaluations," January 31, 1998 (available at http://www.fda.gov/cder/da/patex.17.htm).

yet to be introduced on the market). Drugs already patented by June 8, 1995, may benefit from the change as their manufacturers can choose between the 17-year and 20-year terms and still obtain a Hatch-Waxman extension.[14]

So-called patent pendency periods (the time between applying for a patent and receiving it) vary considerably among drugs. Of the 100 top-selling drugs in 1996, 45 were granted patent-term extensions under the Hatch-Waxman Act. CBO found that the patent pendency period for those 45 drugs averaged 3.3 years.[15] That implies that the new 20-years-from-filing term should have a slightly negative effect for drugs patented after June 8, 1995. The URAA's effect on patent terms interacts with the rules in the Hatch-Waxman Act used to calculate extensions. On net, CBO estimates, those 45 drugs would have lost an average of almost four months of patent life if the 20-years-from-filing term was applied universally.[16]

Companies can file a provisional patent application that establishes priority for their invention but does not start the patent-term clock. They must then file a full application within one year.[17] If companies take advantage of that provisional application, the negative effect of the 20-years-from-filing term could be slightly offset. Firms may also change their behavior in other ways that could speed up the time between patent application and patent grant. For those reasons, CBO assumed in calculating the change in returns from marketing that the URAA had no net impact on effective patent terms.

Some patents that were about to expire under the 17-year term had their expiration dates postponed under the 20-year term established by the URAA. For those patents, a transitional feature in the act allows generic manufacturers to enter a market after the 17-year term expires if the generic manufacturer had already undertaken a substantial investment.[18] However, because of complications in the way the URAA interacts with the Hatch-Waxman Act, that transitional feature does not apply to pharmaceutical products.[19] Some Members tried during the 104th Congress to pass legislation allowing earlier generic entry in the pharmaceutical market in cases in which substantial investment had already been made, but that effort was unsuccessful.

Changes to the Approval Process for Generic Drugs

The Hatch-Waxman Act made two key changes that allow generic manufacturers to obtain FDA approval more quickly once the patent on an innovator drug has expired. First, it established an abbreviated approval process for generic copies of innovator drugs that were approved after 1962. Second, it allowed generic manufacturers to conduct the tests required for FDA approval before the innovator drug's patent expired. Those changes shortened the average time between patent expiration and generic entry for top-selling drugs from three or four years to less than three months. That acceleration of generic entry helps consumers by making lower-cost drugs available more quickly. It also roughly offsets the average 2.8-year delay in generic entry provided by the patent-term extensions and exclusivity provisions in the Hatch-Waxman Act.

Before the act took effect, the FDA had two types of application processes for approving generic copies of innovator drugs. When copying an innova-

14. According to a 1996 ruling by the U.S. Circuit Court, products patented before June 8, 1995, that were already into their Hatch-Waxman extension period on that date are not eligible for the new 20-year patent term under the URAA.

15. Based on data on patent pendency periods provided by Pfizer and data on regulatory review periods and patent-term extensions from the Patent and Trademark Office.

16. Henry Grabowski and John Vernon found that the average patent pendency period for 105 drugs approved between 1990 and 1995 that received Hatch-Waxman extensions was 3.8 years. The overall effect of the URAA, when interacted with the Hatch-Waxman extensions, was a loss of 0.34 years. See Grabowski and Vernon, "Effective Patent Life in Pharmaceuticals," *International Journal of Technology Management* (forthcoming).

17. Title V, section 532(b)(1) of the URAA pertains to provisional applications and the right of priority (see 35 U.S.C. 119(e)(1), 108 Stat. 4985). Section 532(a)(1) defines the new 20-year patent term (see 35 U.S.C. 154(a)(2), 108 Stat. 4984).

18. The generic manufacturer must pay an equitable remuneration to the patent holder (see 35 U.S.C. 154(c)(2) and (3), 108 Stat. 4985).

19. It also does not apply to other products reviewed by the FDA that are eligible for Hatch-Waxman extensions— namely, biological products, food and color additives, and medical devices.

tor drug that had been approved before October 1962, the generic manufacturer had only to demonstrate bioequivalence through clinical tests. When copying an innovator drug approved after 1962, the generic manufacturer also had to demonstrate safety and efficacy. The tests necessary to demonstrate a drug's bioequivalence are much less costly than those required to prove its safety and efficacy.[20] In some instances, the FDA accepted a literature review of published reports in lieu of safety and efficacy tests; such applications were called "paper NDAs."[21] However, in many cases, sufficient evidence was not available in published reports.[22] After the first generic copy of a drug was approved, subsequent applications by generic manufacturers could more easily substitute a literature review for safety and efficacy tests.

In the case of antibiotics, the distinction between pre- and post-1962 drugs did not exist. An abbreviated process for approving generic antibiotics, which required clinical tests to show only bioequivalence, applied to all antibiotic drugs approved under section 507 of the Federal Food, Drug, and Cosmetic Act. Since an abbreviated approval process for generics already existed, such antibiotics were not included in the Hatch-Waxman provisions and were not eligible for patent-term extensions under the act. However, the Food and Drug Administration Modernization Act of 1997 made antibiotic drugs eligible for Hatch-Waxman extensions, thus increasing the returns from their development.

In essence, the Hatch-Waxman Act extended the abbreviated process for approving antibiotics (as well as generic copies of innovator drugs approved before 1962) to all generic drugs. Generic manufacturers now file an abbreviated new drug application, which requires that they perform clinical tests only to demonstrate that their drug is bioequivalent to a drug with an approved NDA that is already on the market. The FDA relies on the safety and effectiveness determination for that original drug when approving the generic copy.

To further speed up the process, the Hatch-Waxman Act explicitly allows generic manufacturers to begin those clinical tests before the original drug's patent expires. In most cases, that change lets manufacturers obtain FDA approval and begin selling copies of an innovator drug soon after patent expiration. Prior to the Hatch-Waxman Act, generic testing occasionally occurred before patent expiration; it was subject to legal dispute until the Court of Appeals for the Federal Circuit ruled in 1984 that such tests infringed on the patent of the innovator drug.[23] The Hatch-Waxman Act effectively reversed that decision by stating that generic manufacturers can begin the FDA approval process before patent expiration. By including the patent expiration date in its application, the generic firm makes explicit its intention not to market the new product until after patent expiration. For its part, the FDA will not approve a new generic drug until the innovator's patent has expired (unless the generic applicant successfully challenges that patent in court).[24]

Before the Hatch-Waxman Act, an average of three to four years elapsed between patent expiration and generic entry. CBO identified 15 cases before 1984 in which one or more generic manufacturers had obtained FDA approval to produce a post-1962 drug by filing a new drug application. For the 11 cases in which a patent expiration date was identified, the average time between patent expiration and generic entry was 3.1 years. In six of those cases, the NDA was applied for before patent expiration. In the other five cases (in which the NDA was applied for after patent expiration), the average time between patent expiration and generic entry was 3.9 years.

20. Grabowski and Vernon, "Longer Patents for Lower Imitation Barriers."

21. See Donald O. Beers, *Generic and Innovator Drugs: A Guide to FDA Approval Requirements*, 4th ed. (Englewood Cliffs, N.J.: Aspen Publishers, 1995), pp. 3-59 to 3-71.

22. House Committee on Energy and Commerce, *Report on the Drug Price Competition and Patent Term Restoration Act of 1984* (June 21, 1984), pp. 16-17. According to that report, the FDA estimated that sufficient published evidence was not available for 85 percent of all post-1962 drugs.

23. The case was *Roche Products, Inc. v. Bolar Pharmaceutical Company, Inc.* (733 F. 2d 858 Federal Circuit 1984). See Alan D. Lourie, "Patent Term Restoration," *Journal of the Patent Office Society*, vol. 66, no. 10 (October 1984), pp. 526-550; and Beers, *Generic and Innovator Drugs*, pp. 4-75 to 4-77.

24. The process for a generic applicant to challenge an innovator's patent is discussed in 21 U.S.C. 355(j)(2)(A)(vii), paragraph IV, and section 355(j)(5)(B)(iii) of the Federal Food, Drug, and Cosmetic Act of 1938, as amended.

For those 15 drugs, generic entry occurred, on average, 1.8 years after the filing of an application. The approval process for those drugs actually took longer than that because before filing an NDA, the generic manufacturers had to research the formulation, contact a chemical manufacturer who could produce the active ingredient, search the literature for preclinical and clinical data, conduct a bioequivalence study, and perhaps demonstrate safety and efficacy as well. Although some of those steps could be taken before patent expiration, the *Roche v. Bolar* decision required that no clinical tests be conducted until afterward.

As an indication of how much more quickly generic entry occurs since the Hatch-Waxman Act, CBO examined 17 brand-name drugs that lost their patent protection between 1990 and 1993, most of which had annual U.S. sales of $50 million or more. For most of those drugs, generic entry occurred within one or two months of patent expiration, although there were exceptions (see Appendix C for more details).[25]

Effects on the Returns from Marketing a Drug

Makers of innovator drugs were slightly worse off after the Hatch-Waxman Act, largely because many more of their drugs experienced generic competition following patent expiration. The act's provision for extending patent terms merely compensated for the loss of the average three-year delay between patent expiration and generic entry that existed before the act (in cases where generic entry occurred).

Still, those extensions played an important role in protecting the returns from drug companies' research and development. Without them, the rise in generic market share since 1984 would have dramatically lowered the expected returns from marketing a drug and might have caused the pharmaceutical industry to reduce its investment in R&D. In that case, a successful innovator drug would have been likely to lose over 40 percent of its market to generic competitors just after reaching its peak year in sales. If the pre-1984 level of R&D investment was desirable, then the patent extensions benefited society by preserving most of the returns from marketing a new drug.

This study uses as a benchmark the average returns from marketing a new drug in the early 1980s under the modest levels of generic entry that existed then. The analysis estimates how much returns have declined relative to that benchmark because innovator drugs (excluding antibiotics) are losing a larger share of their market to generic competitors after patent expiration. Whether the benchmark level of returns is the best one for society is a separate question, which this study does not address.

When a brand-name drug first comes on the market, its sales revenues are low because its benefits are not yet widely known. As the drug becomes better known through published articles, advertising in medical journals, and detailing, its sales rise and reach their peak by year nine or 10, on average. Both before and after 1984, the average innovator drug had a few years of sales at its peak level before generic manufacturers entered the market.

The Hatch-Waxman Act did not greatly change the average point in a drug's life at which generic entry occurs, because the act's patent-term extensions and five-year exclusivity provision together postponed generic entry by roughly the same amount that the act's streamlined approval process sped it up. Two things that did change after 1984 were the likelihood that generics would become available and the average market share captured by generic drugs. Thus, on net, one would expect returns from marketing a new drug to decline after the Hatch-Waxman Act, because although the timing of generic entry has not changed much, the probability of generic entry and the size of the generic market once entry occurs have grown.

Calculating the Change in Returns

CBO estimated the effect of increased generic competition on the stream of profits generated from the sale of 67 innovator drugs that were introduced in the

25. The date of generic entry came from Table 1 of Grabowski and Vernon, "Longer Patents for Increased Generic Competition in the U.S."

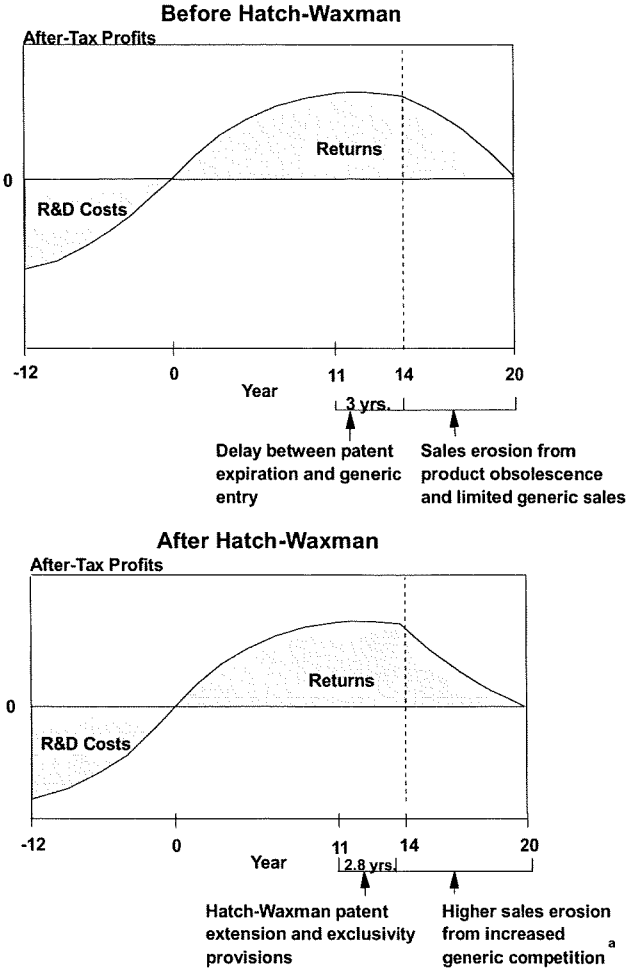
United States in the early 1980s.[26] The data include U.S. sales revenues from 1980 to 1991, covering the first eight to 12 years that those drugs were on the market. The average patent term for the drugs, weighted by sales revenues, was 11 years.

CBO's calculation assumes that the profit stream for an average brand-name drug (excluding antibiotics) would have been the same for the first 11 years with or without the Hatch-Waxman Act. (For more details about the assumptions behind the calculation, see Appendix C.) The total profit stream over the drug's product life is depicted in Figure 7 by the area under the solid curve between year 0 (market introduction) and year 20 (when the drug has become nearly obsolete). The present discounted value of that profit stream, discounted to the date of market introduction, represents the returns from marketing the drug. The negative cash flow before drug introduction represents the investments made in the drug's development. Capitalizing those costs to the date of market introduction brings their total to about $200 million.

For years 12 to 20, CBO estimated two revenue paths, one before and one after the Hatch-Waxman Act. The only difference between those two revenue paths is in the amount of sales revenues lost to competition from generic drugs. Sales revenues also decline in later years because of competition from newer, improved brand-name drugs. CBO assumed that decline to be the same before and after 1984. The pre-1984 path assumes that the drug's patent expires at the end of year 11 but that it takes three years for generics to enter the market, consistent with the data for that period. Therefore, profits do not begin to decline because of generic entry until after year 14. But the decline after year 14 is gradual because generic market share was small for nonantibiotic drugs before 1984.

In the post-1984 path, the Hatch-Waxman Act extends patents by 2.8 years. Generics are assumed to enter about a month later and begin taking a large share of the market. For any specific drug, the size of the generic market and whether generic entry occurs at all will vary. The rate at which profits are eroded depends on whether generic entry occurs and, if so, on the size of the generic market. For the average drug, however, profits erode much more rapidly in this case than before the Hatch-Waxman Act because of greater generic competition. In either case, the effect of increased generic entry on the returns from marketing a

Figure 7.
The Average Profit Stream for a Brand-Name Drug Before and After the Hatch-Waxman Act



SOURCE: Congressional Budget Office.

NOTE: This figure is intended to be illustrative and does not reflect the actual dollar amounts invested in research and development (R&D) or the actual value of profits from drug development.

a. That increased generic competition did not result solely from changes in the Hatch-Waxman Act. Other developments, such as the use of formularies by private-sector health plans to increase generic substitution, also affected the degree to which generic drugs have eroded the profits of off-patent brand-name drugs.

26. Data on average annual U.S. sales of those drugs were provided by Henry Grabowski of Duke University. The analytical approach is based in part on Grabowksi and Vernon, "Longer Patents for Lower Imitation Barriers."

new drug is less than one might expect because generic entry occurs at the end of a drug's product life, when profits are more heavily discounted (in other words, worth less today because they occur farther in the future).

CBO used the actual stream of sales revenues through year 11 for the 67 innovator drugs it examined as the starting point for its calculation. For the pre-1984 profit stream, it applied a rate of sales erosion after generic entry that was based on a sample of 29 top-selling, multiple-source, nonantibiotic drugs in 1980.[27] The erosion rate for the post-1984 case was based on this study's analysis of generic market share in 1993 and 1994.

The total difference between the two profit streams has a present discounted value of $27 million (in 1990 dollars), CBO estimates. In other words, despite the patent extensions and exclusivity provisions in the Hatch-Waxman Act, the growth in generic market share since 1984 has reduced the present discounted value of the returns from marketing a new drug by about $27 million, on average. That figure should be compared with the present discounted value of the total profit stream from marketing an innovator drug throughout its product life, discounted to the date of market introduction, which previous studies have estimated to average $210 million to $230 million for drugs introduced in the 1980s. (Those returns account for production costs but not the capitalized costs of drug development. They include profits from sales abroad, which make up roughly half of total returns.) Expressed as a percentage of those returns, the present discounted value of the returns from marketing a new drug have declined by roughly 12 percent. That result holds true even with modest variations in the assumptions (see the sensitivity analysis in Appendix C).

Grabowski and Vernon and the Office of Technology Assessment estimated that the present discounted value of the returns from marketing a drug exceeded the capitalized costs of R&D by $22 million to $36 million.[28] That is, investment in R&D earned a return slightly higher than the cost of capital, on average. The drugs in those studies did not obtain patent-term extensions under the Hatch-Waxman Act because they were introduced before the act was passed. But they did face increased generic competition once their patents expired. On average, therefore, the returns from marketing a new drug would probably still fully cover the capitalized costs of R&D despite the increase in generic sales since 1984. On the margin, however, a few drugs that were barely profitable to develop would no longer be profitable.

Caveats About CBO's Estimate

CBO's estimated change in returns from marketing a new drug accounts for the full impact of increased generic entry since 1984. But it does not account for many changes in the pharmaceutical market that could increase or decrease those returns, such as changes in R&D costs, in technology, or in the overall demand for prescription drugs. Thus, the estimate is only a partial one, which focuses on the effects of the Hatch-Waxman Act and increased generic sales.

Moreover, since the calculation is based on the U.S. sales of drugs during the 1980-1991 period, it does not include the effects of changes in the pharmaceutical market since then (other than increased generic entry). Some of those changes would raise the returns from marketing a new drug; others would lower them. The rise in managed care since 1991 and its impact on the returns from marketing a new drug are considered only through their effect on increased generic market share. The impact of managed care on the volume of drugs purchased or the prices charged by manufacturers has not been considered. In addition, manufacturers selectively offer discounts and rebates on innovator drugs, but those rebates and some of the discounts are not captured by the data on sales revenues, which are based on average invoice prices.

Other factors not included in the estimate could increase the returns from marketing a new drug. For

27. Masson and Steiner, *Generic Substitution and Prescription Drug Prices*, Appendix A5.

28. Grabowski and Vernon, "Returns to R&D on New Drug Introductions in the 1980s," pp. 383-406; and Office of Technology Assessment, *Pharmaceutical R&D*.

example, the over-65 population, which has a high use of prescription drugs, is growing more rapidly now than it was 10 years ago. In addition, some Medicare beneficiaries are moving into HMOs. Since traditional Medicare does not offer an outpatient drug benefit but many HMOs do, the effect of those moves is to increase prescription drug coverage for the over-65 population.[29] As noted in Chapter 2, managed care techniques may also boost the volume of prescription drugs used by people under 65.

In addition, foreign markets for pharmaceutical products will probably continue to grow as the drug-approval process becomes streamlined in Europe and as various countries strengthen their patent-protection rights.[30] The Agreement on Trade-Related Aspects of Intellectual Property Rights, which was negotiated in 1994 at the Uruguay Round of the General Agreement on Tariffs and Trade, included provisions to encourage developing countries to strengthen their intellectual property rights, particularly in the areas of agriculture and pharmaceuticals. That agreement provides patented pharmaceutical products with a minimum of five years of exclusivity in a participating developing country.[31]

The net effect of changes not accounted for in CBO's estimate may push the total returns from marketing a new drug in one direction or the other. Overall, however, spending on R&D by brand-name manufacturers has increased as a percentage of their sales revenues—from an average of 14.7 percent in 1983 to 19.4 percent in 1995 (despite the fact that such revenues more than tripled).[32] That increase would seem to indicate that, all factors taken together, the incentive to invest in developing new drugs has remained intact since the Hatch-Waxman Act.

No one knows whether that amount of investment in R&D is over or under the optimal level.[33] Some people might argue that companies are not investing enough in drug development and that society would be better off if returns from marketing were increased further. Clearly, the avoided surgery and improved quality of life that result from the use of prescription drugs create large benefits for many people. But it is also possible that too many firms invest in the same research projects, and less could be spent on pharmaceutical R&D without significant costs to society.

Other Considerations

CBO's estimate of the average change in returns from marketing a new drug is small relative to the returns earned on highly successful drugs. The reason is that returns from marketing new drugs are highly skewed. The top six drugs in the set of 67 that CBO used in its calculation earned a return of around $1 billion (discounted to the date of market introduction). But only the top 20 earned a return from marketing that exceeded $200 million, roughly the average cost of drug development.[34] However, since the cost of developing drugs includes the cost of failures, a drug can be profitable in the sense of covering its own development costs but still not earn enough to cover average development costs (which include the cost of drugs that never made it to market). A company must discover a highly profitable drug from time to time for its average returns from marketing to exceed the average capitalized cost of drug development.

Another factor to consider, which can reduce the impact of lower returns, is the so-called replacement effect. When a manufacturer introduces a new brand-name drug, that drug may erode the sales of similar drugs the company already has on the market. CBO's

29. In 1997, 4.5 million out of 38.2 million Medicare beneficiaries were enrolled in an HMO or risk-based health plan. CBO projects that the proportion of Medicare beneficiaries enrolled in such plans will continue to grow. See Congressional Budget Office, *The Economic and Budget Outlook: Fiscal Years 1999-2008* (January 1998), Appendix F.

30. Standard & Poor's, *Healthcare: Pharmaceuticals*, Industry Surveys (New York: Standard & Poor's, August 29, 1996), p. 21.

31. See Dorothy Schrader, *Intellectual Property Provisions of the GATT 1994 and the Uruguay Round Agreements Act*, CRS Report for Congress 94-302A (Congressional Research Service, September 23, 1996), pp. 36-37.

32. Pharmaceutical Researchers and Manufacturers of America, *1997 Industry Profile* (Washington, D.C.: PhRMA, March 1997), p. 57. Those figures equal R&D spending in the United States divided by domestic sales plus exports.

33. See F.M. Scherer, "Pricing, Profits and Technological Progress in the Pharmaceutical Industry," *Journal of Economic Perspectives*, vol. 7, no. 3 (Summer 1993), p. 111.

34. Grabowski and Vernon, "Returns to R&D on New Drug Introductions in the 1980s," pp. 398-400.

estimate of the decline in the present discounted value of the returns from marketing a new drug does not consider the dynamic effect of such product replacement. The replacement effect derives from the reduced incentive that companies have to innovate when a new drug will replace a share of the market currently held by one of their other products. (For more details about that effect, see Appendix D.) The rise in generic market share, however, reduces the replacement effect. A firm has less to lose by replacing an older product with a new drug when the patent on the older product is about to expire, since generics will take away a large share of that product's market anyway.

An example is the allergy drug Allegra, introduced in 1996 by Hoechst Marion Roussel, which also sells a competing brand-name drug, Seldane. The two drugs are very similar antihistamines, but Allegra has fewer negative side effects. Because of the replacement effect, Hoechst Marion Roussel had less incentive to introduce Allegra when it would cut into the profits from the sale of Seldane significantly. However, anticipation of generic competition reduced that replacement effect—Allegra was introduced just three years before Seldane's patent was to expire.[35]

Although the growth of generic competition since 1984 has reduced the returns from innovation overall, the effect of those lower returns on the incentive to innovate will be offset somewhat by a commensurate reduction in the replacement effect. That is, the slightly reduced value of profits at the end of a drug's product life will give firms with existing products a greater incentive to replace them in the market more quickly—as close to patent expiration as possible.

That dynamic effect exists only when pharmaceutical firms continue to invest in developing drugs in therapeutic areas where they are already market leaders. Large firms usually conduct R&D in a variety of therapeutic areas, so the dynamic effect will be greater for some projects and nonexistent for others.[36] The operation of the replacement effect reduces—but does not eliminate—the negative impact that the rise in generic market share has on the incentive to invest in developing brand-name drugs.

Effects of Proposed Changes to the Hatch-Waxman Act

Some representatives of the pharmaceutical industry would like to modify the Hatch-Waxman Act in various ways to increase the average effective patent term for pharmaceutical products.[37] Although lengthening patents would increase profits today for drugs whose patents are expiring, it would not have as large an impact on the incentive to invest in R&D—that is, on the present discounted value of the returns from marketing a new drug. Extending the average effective patent term by one year would increase the present discounted value of those returns by about $12 million.

In contrast, accelerating the FDA review period by one year would have a much greater effect on the present discounted value of the returns from marketing a new drug—a net benefit of about $22 million, on average. Thus, reducing FDA approval times—if it could be done without sacrificing safety concerns—would be much more effective in helping both the drug industry and consumers than would lengthening the patent-protection period.

Some drugs do not benefit from patent-term extensions because they have no patent to extend, or because their patent has already expired (perhaps because the drug lingered in the clinical testing phase). Lengthening the five-year exclusivity period for a new drug (that contains a chemical entity never before approved) would have a sizable impact on the incentive to develop those drugs, because the benefits would be

35. Department of Health and Human Services, Food and Drug Administration, *Approved Drug Products with Therapeutic Equivalence Evaluations* (1997). The section that contains patent expiration dates and exclusivity periods is available at http://www.fda.gov/cder/da/patex17.htm. Seldane's patent expires in April 1999; Allegra was introduced in July 1996.

36. For a discussion of the diversity of R&D projects within a single firm and the benefits of such diversification, see Rebecca Henderson and Ian Cockburn, "Scale, Scope and Spillovers: The Determinants of Research Productivity in Drug Discovery," *RAND Journal of Economics*, vol. 27, no. 1 (Spring 1996).

37. See testimony at the Senate Judiciary Committee's hearing on the Hatch-Waxman Act on March 5, 1996.

seen relatively early in the drug's product life. Furthermore, the current exclusivity period is probably too short to compensate for the average cost of developing those drugs. Out of the 101 drugs approved between 1992 and 1995, 10 would have benefited from a lengthening of the five-year exclusivity period.

Conclusions

The Hatch-Waxman Act eliminated the duplicative testing requirements for manufacturers of generic drugs to obtain FDA approval. That regulatory relief has translated into greater availability of generic drugs and lower average prices to consumers for off-patent drugs. By itself, the doubling of generic market share between 1984 and 1994 would have substantially lowered the returns from marketing new innovator drugs. However, the act also provided patent extensions that postponed the time when an innovator drug would face generic competition.

CBO's analysis has found that the patent extensions available under the Hatch-Waxman Act were not sufficient to fully preserve the returns from marketing new brand-name drugs. The present discounted value of those returns has declined by about 12 percent because of the rise in generic competition. However, that rise has resulted from a variety of demand-side factors as well as from changes in the act itself.

The Hatch-Waxman Act helped increase the opportunity to substitute less expensive generic drugs for more expensive off-patent brand-name drugs. That substitution lowers the average cost of a multiple-source prescription drug. The point in the life of an average drug at which generic entry occurs did not change much under the act, because the average length of a patent extension roughly offsets the average delay between patent expiration and generic entry that existed before 1984. Of course, that specific timing varies significantly from one drug to another. Nevertheless, many purchasers are better off since the act, as most top-selling off-patent brand-name drugs now have generic versions available. And with the lower testing costs required for FDA approval, more generic manufacturers probably find it profitable to enter a given market. Empirical evidence suggests that that puts downward pressure on the average prescription price of generic drugs as well.

Many changes in the pharmaceutical market and in the technology of drug development have affected the returns from marketing a new drug. This study considered only two changes that affect those returns: the increase in generic market share since 1984 and the increase in patent terms under the Hatch-Waxman Act. Changes that were not considered may, taken together, either increase or decrease those returns. Overall, it appears that the incentives for drug companies to innovate have remained intact since the Hatch-Waxman Act; even as sales revenues from innovator drugs have more than tripled, the percentage of those revenues that manufacturers reinvest in R&D has risen from 14.7 percent to 19.4 percent between 1983 and 1995.

Appendixes

Appendix A

Data Used for the Empirical Estimates

This study draws on several different sets of data that cover sales revenues, prices, and quantities for prescription drugs sold in the United States (see Table A-1 for an overview). The data come from two private companies that collect and sell information about the pharmaceutical industry (Scott-Levin and IMS America), from three government agencies (the Food and Drug Administration, the Patent and Trademark Office, and the Health Care Financing Administration), and from Henry Grabowski, an economist at Duke University.

Retail Pharmacy Data Set

Many of the estimates in Chapter 3 rely on a set of retail pharmacy data purchased from Scott-Levin. That data set covers the number of prescriptions dispensed at retail pharmacies in 1993 and 1994 for all formulations of all prescription drugs in 66 narrowly defined therapeutic classes, as well as the revenues from sales of those drugs, valued at retail prices. (Those retail prices are the average of the actual retail transaction prices charged by pharmacies.) The total value of sales revenues in the data set equals approximately 70 percent of the total sales revenues of retail pharmacies in the United States from prescription drugs. The data set is based on Scott-Levin's Source Prescription Audit, which covers more than 34,000 U.S. retail pharmacies. Scott-Levin projects the sales data upward to reflect sales through all pharmacies in the United States (which numbered 67,939 in 1995).[1] Since retail pharmacies distribute roughly half of the value of prescription drugs, this data set represents approximately 35 percent of the value of all prescription drug sales in the nation.

The data are broken down by each dosage form of each drug in the 66 therapeutic classes. For example, if a multiple-source drug comes in both 50 milligram and 100 milligram tablets, the data set includes the sales revenues and number of prescriptions for each brand-name and generic manufacturer (if there are any) of both of those dosage forms. The set contains 454 different prescription drugs (or chemical entities), 177 of which are multiple source. Expanding that by the different dosage forms for each drug—many of which are produced by several manufacturers—brings the number of individual observations in the data set to 11,665. The Congressional Budget Office (CBO) added the chemical names of the brand-name drugs (using the reference book *Drug Facts and Comparisons*) and coded each observation so the generic drugs could be matched with their brand-name counterparts.[2]

1. National Association of Boards of Pharmacy, *Survey of Pharmacy Law: 1995-1996* (Park Ridge, Ill.: National Association of Boards of Pharmacy, 1995), p. 90.

2. Facts and Comparisons, *Drug Facts and Comparisons* (St. Louis: Facts and Comparisons, 1995).

Table A-1.
Data and Methods Behind CBO's Estimates

Empirical Estimate	Data Used	Method
Average prescription price and market share for brand-name and generic drugs (Chapter 3, Table 1)	Retail pharmacy sales data purchased from Scott-Levin. Includes the number of prescriptions dispensed through retail pharmacies for 11,665 dosage forms of 454 drugs.	The total retail pharmacy sales revenues for a given type of drug were divided by the number of prescriptions dispensed for it. The drug types are multiple-source and single-source brand-name drugs and generic drugs. Market share is the percentage of total prescriptions dispensed for that type of drug.
Market concentration by therapeutic class (Chapter 3, Figure 5)	Retail pharmacy data set	The percentage of sales held by the top three brand-name drugs was calculated for 66 therapeutic classes.
Price differences for various types of purchasers (Chapter 3, Table 4)	Computed by IMS America based on invoice prices to most intermediate purchasers, such as pharmacies (other than mail-order ones), clinics, hospitals, and HMOs. Prices are net of invoice discounts but do not include rebates.	For 100 top-selling outpatient drugs, the average prices paid by intermediate purchasers are expressed as a percentage of the average price paid by pharmacies.
Effect of competition on manufacturers' discounting of brand-name drugs sold to intermediate purchasers (Chapter 3)	Average manufacturer price to pharmacies and lowest price to any U.S. purchaser as reported to HCFA under the Medicaid rebate program. The number of brand-name manufacturers in the therapeutic class and the existence of generic formulations were obtained from the retail pharmacy data set. Total Medicaid sales were obtained from HCFA and total U.S. sales from IMS America.	Regression analysis (see Appendix B for more details). The dependent variable is the lowest price to any intermediate purchaser divided by the average price to pharmacies. Explanatory variables include the number of brand-name manufacturers in the drug's therapeutic class, a dummy variable taking the value of 1 when generic forms are available, and the drug's Medicaid market share.
Percentage change in brand-name drug prices between 1991 and 1994 (Chapter 3)	The average manufacturer price to pharmacies, reported by manufacturers to HCFA under the Medicaid rebate program. Price is reported per unit, such as tablet, and is equal to total sales divided by the number of units sold in a given quarter. Those prices include most discounts and rebates to pharmacies. Whether a given drug had generic competitors was determined from the retail pharmacy data set.	Calculated the average percentage change in price between 1991 and 1994 for 269 brand-name drugs. Compared those facing generic competition with those not facing generic competition.

Table A-1.
Continued

Empirical Estimate	Data Used	Method
Total direct savings from generic substitution on retail pharmacy prescriptions (Chapter 3)	Retail pharmacy data set; 177 of the 454 drugs in the data set were multiple source in 1993 and 1994. CBO coded the data to link each brand-name drug with its generic competitors.	For each multiple-source drug, the difference between the brand-name and generic retail price for a prescription was multiplied by the number of generic prescriptions of the drug purchased through pharmacies in 1994. That difference was then summed for all multiple-source drugs.
Decline in average generic prescription price as the number of manufacturers rises (Chapter 3, Table 5)	Retail pharmacy data set	The average generic prescription price was calculated for cohorts of generic drugs, grouped by the number of generic manufacturers. The average ratio of generic to brand-name prescription price was also calculated by cohort.
Average length of patent-term extensions under the Hatch-Waxman Act (Chapter 4, Table 8)	Extension length was obtained from the PTO for the 51 drugs approved by the FDA between 1992 and 1995 that received an extension.	Averages were calculated for the 51 drugs approved between 1992 and 1995 that received an extension and for all new drugs approved during that period.
Effects of increased generic competition and longer patent terms on the returns from marketing a new drug (Chapter 4)	Average U.S. manufacturer sales of 67 brand-name drugs over their product life, obtained from Henry Grabowski. Those drugs were introduced between 1980 and 1984. The average is based on actual sales for the first eight to 12 years that a drug was on the market; remaining years were projected.	Calculated the change in the present discounted value of the profit stream for the average drug when the rise in generic market share and the Hatch-Waxman extensions are considered together (see Appendix C for more details).
	Retail pharmacy data set	The rate of sales erosion from generic competition after the Hatch-Waxman Act is based on analysis of 21 drugs that lost patent protection between 1991 and 1993 (for the first year's rate) and all off-patent drugs in the data set (for the rate in subsequent years).

SOURCE: Congressional Budget Office.

NOTE: HMOs = health maintenance organizations; HCFA = Health Care Financing Administration; PTO = Patent and Trademark Office; FDA = Food and Drug Administration.

CBO used that data set to estimate the total savings on prescriptions at retail pharmacies from generic substitution, to compare retail pharmacy sales of generic and brand-name drugs, and to analyze generic competition. Portions of the data set were also used to examine market concentration at the level of the therapeutic class for brand-name drugs and at the level of a single multiple-source drug for generics.

One drawback of the data set is that prescriptions are not the best measure of the quantity of sales. When comparing the prices of two drugs, the best comparison is one based on the price of an average daily dose, not the price of a prescription. Because prescriptions for a drug are typically dispensed in a variety of sizes (the quantity of dosage units, such as pills, varies), comparisons between them are potentially misleading. The variability in prescription sizes may be more of a problem for chronic drugs—which are taken over a long period of time—than for acute drugs. In the case of chronic drugs, whether a pharmacist dispenses a prescription that will last one month or four months may be arbitrary. However, since the data set covers such a large number of prescriptions, it seems reasonable to assume (where relevant) that the average quantity dispensed per prescription for one type of drug will be roughly equivalent to the average quantity dispensed for a close competitor. Moreover, such an assumption is necessary for carrying out any quantitative analysis because of the lack of better data.

CBO used prices per prescription to evaluate the reduction in prescription drug spending from generic substitution and the relative prices of brand-name and generic drugs. Those data were also used to evaluate the decline in the average prescription price as the number of generic manufacturers rises. The measurement error inherent in using a prescription as the unit of quantity could cause the estimated price difference between a brand-name drug and its generic counterpart to be either too high or too low—depending on whether generic prescriptions are smaller or larger, on average, than their brand-name counterparts. Consequently, the estimates of average prescription prices and of the savings to consumers from generic substitution should be viewed as rough figures, not exact ones.

All of the estimates based on average prescription prices cover only tablet and capsule dosage forms, which constitute 87 percent of all sales (or 91 percent of generic sales) in the data set. The average prescription price for those dosage forms appears more reliable than the average price when injectable and liquid dosage forms are included.

Total U.S. Sales at Average Invoice Prices

CBO purchased data on the total U.S. sales of 350 prescription drugs from IMS America. That data set covers all channels of distribution except mail-order pharmacies. The sales revenues are valued at the average prices charged on invoices to hospitals, pharmacies, and other purchasers. IMS America also calculated the difference in average invoice prices paid by different channels of distribution for 100 top-selling drugs that were largely distributed through retail pharmacies.

As discussed in Chapter 3, the average invoice price does not include rebates and some discounts that manufacturers give purchasers. As a result, the average invoice price slightly overstates the final price paid. Pharmaceutical Research and Manufacturers of America estimates that discounts and rebates (not including Medicaid rebates) amounted to about $3.5 billion in 1994. Assuming that none of those discounts and rebates were included on an invoice, that figure would equal 5.5 percent of total pharmaceutical sales valued at invoice prices. Although the excluded discounts and rebates are small overall, they could substantially alter the price dispersion figures in Chapter 3 if they were disproportionately received by a particular type of purchaser.

The calculation of the change in returns from marketing a new drug was based on data provided by Henry Grabowski for the average annual U.S. sales revenues of 67 brand-name drugs (valued at invoice prices). Those drugs were introduced between 1980 and 1984. The sales data cover the 1980-1991 period

and thus capture the first eight to 12 years that those drugs were on the market. For drugs with only eight to 10 years of actual data, CBO relied on sales projections by Grabowski and John Vernon to determine average annual sales revenues through year 11 for all 67 drugs.

Pricing Data from the Medicaid Rebate Program

CBO obtained data from the Health Care Financing Administration (HCFA) on the average price that manufacturers charge wholesalers for drugs that are then distributed through retail pharmacies, as well as on the lowest price charged to any private purchaser (known as the best price). Manufacturers are required by the Medicaid rebate program to report those prices to HCFA for all brand-name drugs that Medicaid beneficiaries buy at retail pharmacies. CBO also obtained data on total Medicaid sales by prescription drug (valued at the price at which states reimburse pharmacies for purchases through Medicaid). Those data were used to assess the differences in price increases between 1991 and 1994 for multiple-source and single-source brand-name drugs.

Those prices reported to HCFA are among the best available (although they are not publicly available) to assess price changes for drugs channeled through retail pharmacies. They represent actual transaction prices, since all discounts and rebates to wholesalers and retail pharmacies are included. Both the average price to pharmacies and the best price are reported by dosage units, such as price per 50 milligram tablet. The average price to pharmacies of a particular dosage form of a drug is calculated by dividing the value of its total sales to wholesalers or chain pharmacies by the number of dosage units sold.[3]

Data from the Patent and Trademark Office and the FDA

The Patent and Trademark Office provided data on all drugs approved through 1995 that have received an extension under the Hatch-Waxman Act. The Food and Drug Administration (FDA) provided overlapping data on the average length of time those drugs spent in clinical testing and in having their new drug applications approved. Those data were used to calculate the average length of a Hatch-Waxman extension and the average time a drug spends in the FDA approval process.

3. Details on how the best price and average manufacturer price are calculated can be found on HCFA's Web site at http://www.hcfa.gov/medicaid/drug8.htm.

Appendix B

Regression Results on Discounting

The Congressional Budget Office (CBO) analyzed whether the discounts that manufacturers offer on brand-name prescription drugs tend to be greater when several therapeutically similar brand-name drugs or generic copies are available. The analysis is based on the difference between the average price that manufacturers charge for a particular brand-name drug distributed through retail pharmacies (the average manufacturer price to pharmacies) and the lowest price they charge to any private purchaser in the United States for that drug (the best price). The percentage difference between those two prices is called the best-price discount. CBO's analysis shows that best-price discounts are indeed greater when more competing brand-name or generic substitutes for a drug are available.

That result suggests that discounts are a response to competitive market forces. Discounting may in fact be an important component of price competition in the pharmaceutical market, but because of limited data, CBO cannot gauge its prevalence. This analysis is based on pricing data that only measure the size of the largest discounts offered to private purchasers on brand-name drugs. The quantity of brand-name drugs sold at those discounts, or any discount, is unknown. Therefore, these results are only suggestive.

The Dependent Variable

In CBO's regression analysis of discounting, the dependent variable (that is, the value to be explained) is the ratio of the best price to the average manufacturer price for a given brand-name drug sold through retail pharmacies. (Frequently, such drugs are sold to wholesalers rather than directly to pharmacies.) If a brand-name drug is always sold at the same price, that ratio will equal 1; if it is ever sold at a discount, the ratio will be less than 1.

Manufacturers report best prices and average prices to pharmacies to the Health Care Financing Administration as part of the Medicaid rebate program.[1] The average manufacturer price to pharmacies includes all discounts and rebates given to retail pharmacies. That average is calculated by dividing all sales of a particular dosage form of a brand-name drug to retail pharmacies (after netting out all applicable discounts and rebates) by the number of units of that dosage form sold to retail pharmacies (including mail-order pharmacies). That price is therefore an average transaction price. The best price also includes all discounts and rebates given to any private purchaser. Under the Medicaid rebate program, Medicaid is entitled to receive a discount equal to the best-price discount or 15.1 percent of the average manufacturer price to pharmacies, whichever is greater.

1. The amount that manufacturers sell at the best price is not known. However, Medicaid's best-price provision helps ensure that a significant quantity is sold at that price. Offering a very low price on an extremely small quantity is usually unprofitable for a company because it increases the rebate on all outpatient sales to Medicaid. For more details on the pricing data set and the Medicaid rebate program, see Congressional Budget Office, *How the Medicaid Rebate on Prescription Drugs Affects Pricing in the Pharmaceutical Industry*, CBO Paper (January 1996).

To isolate the effects of competition on price dispersion, and to adjust for other factors that may affect prices, CBO selected a set of economic and therapeutically relevant variables for its regression. It used multivariate statistical analysis to analyze the effects of those variables on the ratio of the best price to the average price to pharmacies (BP/AP) for a particular brand-name drug. The explanatory variables for market competition—which include the number and types of substitutes that compete with a particular brand-name drug—are based on CBO's retail pharmacy data set, which covers sales through retail pharmacies of all drugs in 66 narrowly defined therapeutic classes in 1994. Those 66 therapeutic classes encompassed 70 percent of all retail pharmacy sales in 1994. The regression was run using pricing data for the fourth quarter of 1994 and the competitive market variables constructed from the retail pharmacy data set for calendar year 1994.

The Explanatory Variables

The analysis used six explanatory variables (see Table B-1 for a description of them, along with their means and ranges). The variable explaining brand-name competition is defined at the level of a drug's five-digit therapeutic class, as established by the Uniform Standard of Classification codes (see Box 3 on page 23). That variable, INVNMBR, the inverse of the number of manufacturers, is equal to 1 divided by the number of manufacturers of brand-name drugs in a five-digit therapeutic class. That variable resembles imperfect competition based on a Cournot model, in which the equilibrium price is a function of 1/(N+1), N being the number of manufacturers. (In that model, firms choose the profit-maximizing quantity to produce, and the equilibrium price results. Note that the Cournot model does not apply when N = 1).

Another model of imperfect competition that could apply to the pharmaceutical industry is Bertrand competition with limited entry and differentiated products. In that model, firms compete by setting prices, with prices declining as the number of firms in a therapeutic class increases.[2] Specifically, the ratio BP/AP should decline as the market becomes more competitive if the difference in cross-price elasticities between pharmacies and other types of purchasers grows as more substitutes are introduced. Previous theoretical analyses and one empirical study have shown that the gap in prices paid by different types of purchasers widens with increased competition when the difference in price sensitivity among types of purchasers grows as more substitutes are introduced.[3]

Manufacturers are more likely to offer discounts when there are more similar brand-name drugs in the same therapeutic class. A manufacturer has less incentive to offer a discount on a breakthrough drug that has no close substitutes. With respect to the dependent variable, the best price should be closest to the average price to pharmacies when there is only one manufacturer of a brand-name drug in a given therapeutic class. Larger values of the BP/AP ratio should be associated with larger values of INVNMBR; thus, the expected sign of the coefficient on INVNMBR is positive.

Similarly, the difference between the average price to pharmacies and the best price should increase when generic manufacturers are producing copies of the brand-name drug. The variables explaining generic competition are GENDUM (a dummy variable) and INVNMG (the inverse of the number of generic

2. Four functional forms for competition were tried: the log of N, (N+N*N), N, and 1/N. Although the coefficients took the expected signs in all four cases, only 1/N yielded statistically significant results for both brand-name and generic competition. This functional form for competition was also used by Wiggins and Maness to explain price competition in antibiotic markets. See Steven Wiggins and Robert Maness, "Price Competition in Pharmaceutical Markets" (working paper, Texas A&M University, Department of Economics, June 1994). The empirical analysis does not distinguish whether Bertrand competition or Cournot competition is the more appropriate model for the pharmaceutical industry.

3. Thomas J. Holmes, "The Effects of Third-Degree Price Discrimination in Oligopoly," *American Economic Review*, vol. 79 (March 1989); Severin Borenstein, "Price Discrimination in Free Entry Markets," *Rand Journal of Economics*, vol. 16, no. 3 (Autumn 1985); and Severin Borenstein and Nancy L. Rose, "Competition and Price Dispersion in the U.S. Airline Industry," *Journal of Political Economy*, vol. 102, no. 4 (1994).

Table B-1.
Variables Used in the Regression Analysis of Discounting

Variable	Description	Mean	Range
	Dependent Variable		
BP/AP	The ratio of the best price (the lowest price to any private purchaser in the United States) for a brand-name drug relative to the average price to pharmacies.[a] The prices for the top-selling dosage form of each brand-name drug were used.	.77	.10 to 1
	Explanatory Variables		
INVNMBR	The inverse of (or 1 divided by) the number of manufacturers in a therapeutic class producing an innovator drug.	.23	.08 to 1
	Number of brand-name manufacturers per class:	6.3	1 to 13
GENDUM	Dummy variable that takes the value of 1 if generic entry has occurred and 0 otherwise. A threshold of $1 million in total generic sales must exist for this variable to take a value of 1.	n.a.	0 to 1
INVNMG	The inverse of the number of generic manufacturers and distributors of a bioequivalent formulation of the brand-name drug. This term is interacted with GENDUM so it takes a value of 0 if GENDUM is 0 and 1 divided by the number of generic manufacturers if GENDUM is 1.	.20[b]	.04 to 1[b]
	Number of generic manufacturers per brand-name drug:	11.0[b]	1 to 24[b]
MDSHARE	Medicaid's market share for a brand-name drug, defined as total Medicaid sales of the drug divided by its total U.S. sales.	.14	.0005 to .79
CLSDUM	A dummy variable for each therapeutic class defined at the broader two-digit level under the Uniform Standard of Classification codes. The data set contained 26 therapeutic classes at the two-digit level, 25 of which received a dummy. (The class left out was respiratory drugs.)	n.a.	0 to 1
MNDUM	A dummy variable given to each manufacturer of a brand-name drug that had nine or more products in the sample. There were 14 such manufacturers.	n.a.	0 to 1

SOURCE: Congressional Budget Office.

NOTE: n.a. = not applicable.

a. This price is reported by manufacturers as the average price charged on sales to the retail pharmacy class of trade (it does not include the wholesaler's markup). The price is calculated by dividing total manufacturer sales to the retail pharmacy class of trade by the quantity sold (that is, the number of dosage units, such as tablets).

b. Mean and range were taken over those observations in which GENDUM equals 1.

manufacturers). GENDUM takes a value of 1 if a generic form of the brand-name drug is available. The expected sign of the coefficient on GENDUM is negative since the best price should tend to be lower relative to the average price to pharmacies when a generic drug is available.

The variable INVNMG is interacted with GENDUM, taking the value of 1 divided by the number of generic manufacturers and distributors (with retail sales of $100,000 or more) when GENDUM equals 1 and taking the value of 0 when GENDUM equals 0. Larger values of INVNMG are associated with fewer generic manufacturers and therefore less competition. Thus, larger values of INVNMG are associated with higher values of BP relative to AP, and the expected sign on this variable is positive. When there are four generic manufacturers, GENDUM and INVNMG together yield (1)*GENDUM + 0.25*(INVNMG) < 0 as long as the expected sign on GENDUM dominates.

Medicaid market share was included as an explanatory variable (MDSHARE) because of the provision in Medicaid's rebate program that requires manufacturers to pay a larger rebate to Medicaid if they offer a price to any private purchaser that is more than 15.1 percent (15.4 percent in 1994) below the average price to pharmacies. Since Medicaid constitutes a large share of the retail pharmacy market—about 13 percent on average—that provision discourages manufacturers from offering large discounts. Medicaid market share varies widely among different types of drugs, and the larger Medicaid's share in a particular drug's market, the less incentive that manufacturer has to offer a large discount.[4] Therefore, the expected sign on this coefficient is positive, since a larger Medicaid market share will be associated with less difference between the best price and the average price to pharmacies.

To account for differences in the marginal cost of production between therapeutic classes, as well as competitive market characteristics not accounted for in the explanatory variables, the analysis included therapeutic-class dummies at the two-digit level (CLSDUM). And to account for possible differences in pricing policies between manufacturers, those manufacturers with at least nine brand-name drug observations in the data set were given a dummy variable (MNDUM).

The Results

The coefficients on INVNMBR, GENDUM, and MDSHARE are all significant at the 1 percent level, and the coefficient on INVNMG is significant at the 5 percent level (see Table B-2).[5] All four coefficients have the expected signs. Four of the manufacturer dummies and 12 of the class dummies are also significant at the 5 percent level.[6]

The coefficients on GENDUM and INVNMG together imply that when two generic manufacturers have entered a market, the BP/AP ratio is 10 percentage points lower, and when three or more generic manufacturers have entered that market, the BP/AP ratio is 12 to 17 percentage points lower (see Table B-3). That implies that discounts are larger when a generic drug is available, and the size of the discounts increases as more generic manufacturers enter the market.

The regression results also show that competition from other brand-name drugs can increase price dispersion. When there are three or more manufacturers of brand-name drugs in a therapeutic class, the BP/AP ratio is 10 to 14 percentage points lower than if there was only one brand-name manufacturer in that class. Moving from one to two brand-name manufacturers is a particularly important step, as the BP/AP ratio declines by 8 percentage points. Each subsequent brand-name entrant continues to reduce that ratio by a small amount. The more brand-name manufacturers in a class, the greater the difference between the best price

4. See Congressional Budget Office, *How the Medicaid Rebate on Prescription Drugs Affects Pricing in the Pharmaceutical Industry*.

5. A statistical test (the Goldfeld-Quandt test) showed heteroscedasticity. The error terms tend to be larger when MDSHARE is small. The standard errors were corrected for heteroscedasticity before calculating the statistical significance of the estimated parameters.

6. A chi-square test of the hypothesis that the coefficients of the set of manufacturer dummies are jointly equal to zero can be rejected with 99 percent probability. And a similar test of whether the coefficients of the set of class dummies are jointly equal to zero can be rejected at the same probability level. Those results indicate that accounting for differences among manufacturers and between therapeutic classes is important in explaining changes in BP/AP.

Table B-2.
Regression Results on Price Dispersion in 1994

Explanatory Variable	OLS Parameter Estimate	Standard Error[a]	t Statistic[b]
Intercept	0.650**	0.0560	11.61
INVNMBR	0.145**	0.0532	2.73
GENDUM	-0.172**	0.0351	-4.90
INVNMG	0.154*	0.0778	1.97
MDSHARE	0.358**	0.0942	3.79
clsdum1	0.185	0.0927	1.99
clsdum2	0.171*	0.0782	2.19
clsdum3	0.234**	0.0587	3.98
clsdum4	0.174**	0.0699	2.48
clsdum5	0.108**	0.0527	2.05
clsdum6	0.045	0.1146	0.39
clsdum7	-0.006	0.0773	-0.08
clsdum8	0.151*	0.0627	2.41
clsdum9	0.019	0.0520	0.37
clsdum11[c]	0.248**	0.0533	4.65
clsdum12	0.225**	0.0860	2.62
clsdum13	0.111*	0.0526	2.11
clsdum14	0.157	0.0991	1.58
clsdum15	-0.126	0.1254	-1.01
clsdum16	-0.157	0.0972	-1.62
clsdum17	0.163*	0.0766	2.12
clsdum18	0.083	0.0960	0.87
clsdum19	0.144**	0.0515	2.79
clsdum20	-0.003	0.0813	-0.04
clsdum21	0.041	0.1170	0.35
clsdum22	0.124	0.0851	1.46
clsdum23	0.127*	0.0627	2.03
clsdum24	0.086	0.1243	0.69
clsdum25	0.213**	0.0526	4.05
clsdum26	0.107	0.0815	1.31
mndum1	-0.180*	0.0691	-2.60
mndum2	0.012	0.0414	0.29
mndum3	0.005	0.0454	0.11
mndum4	-0.033	0.0709	-0.46
mndum5	0.016	0.0670	0.23
mndum6	-0.013	0.0592	-0.22
mndum7	0.188**	0.0390	4.81
mndum8	-0.102	0.0593	-1.73
mndum9	-0.216**	0.0819	-2.63
mndum10	-0.012	0.0427	-0.27
mndum11	-0.124*	0.0609	-2.04
mndum12	-0.067	0.0601	-1.11
mndum13	0.109	0.0782	1.39
mndum14	-0.142	0.0816	-1.74

SOURCE: Congressional Budget Office.

NOTES: The dependent variable is the ratio of the best price to the average price to pharmacies. The R squared is 0.32 and the adjusted R squared is 0.22. The results are for the fourth quarter of 1994; there were 327 observations.

OLS = ordinary least squares; * = significant at the 5 percent level; ** = significant at the 1 percent level.

a. The Goldfeld-Quandt test showed that heteroscedasticity is present. The standard errors were corrected using a consistent covariance matrix.

b. The t statistic was calculated using the corrected standard errors. The statistical significance of the five leading coefficients was confirmed using a chi-square test.

c. Clsdum10 was omitted. That class represents respiratory drugs.

Table B-3.
The Effects of Generic and Brand-Name Competition on Price Dispersion

Number of Manufacturers	Change in Ratio of Best Price to Average Pharmacy Price (BP/AP)
Competition from Generic Drugs	
1	-0.02
2	-0.10
3	-0.12
4	-0.13
5	-0.14
6 to 8	-0.15
9 to 21	-0.16
22 to 24	-0.17
Competition from Other Brand-Name Drugs	
1	0.15
2	0.07
3	0.05
4	0.04
5	0.03
6 to 9	0.02
10 to 13	0.01

SOURCE: Congressional Budget Office.

and the average price, which implies that discounts are larger.

The coefficient on Medicaid market share indicates that at the mean market share of 13 percent, the BP/AP ratio is 4.6 percentage points higher because of Medicaid's best-price provision. If Medicaid has just 5 percent of the market, then the BP/AP ratio is just 2 percentage points higher, and if Medicaid has 30 percent of the market, that ratio is 11 percentage points higher. As expected, a larger Medicaid market share is associated with less price dispersion.[7]

7. The same regression was run using the BP/AP ratio for the fourth quarter of 1993. The variables GENDUM, INVNMG, INVNMBR, and MDSHARE were constructed based on 1993 annual sales. The coefficients on those variables and the intercept obtained from the 1993 regression did not differ with statistical significance from the values of those coefficients shown in Table B-2 (based on a chi-square test). Nor does the difference in the values of the coefficients obtained from the 1993 regression change the economic interpretation of those coefficients. The coefficient that changed the most between the two regressions was INVNMG. According to the 1993 regression, if two or more generic manufacturers enter the market, the BP/AP ratio declines by 7 to 20 percentage points.

Appendix C

Assumptions Behind the Calculation of Returns from Marketing a New Drug

Despite the patent extensions included in the Hatch-Waxman Act, the present discounted value of the average returns from marketing a new drug have fallen by an estimated $27 million, or approximately 12 percent, because of the increase in generic market share since 1984. That calculation, presented in Chapter 4, employs a methodology used by economists Henry Grabowski and John Vernon in various analyses and by the Congressional Budget Office (CBO) in a 1994 study of returns from research and development in the pharmaceutical industry.[1] The calculation is based on estimates obtained from this study's analysis of generic entry after patent expiration. Assumptions similar to the ones in CBO's 1994 study were used to convert the change in the stream of sales revenues to the change in profits.

The key assumptions in the calculation—the rate at which sales revenues eroded before and after the Hatch-Waxman Act and the change in the length of patent protection—are based on analysis of CBO's retail pharmacy data set, data on patent extensions from the Patent and Trademark Office, and a study by the Federal Trade Commission.[2] The change in returns is calculated by projecting the value of total U.S. sales revenues in the 12th to 20th year after market introduction for the average drug in CBO's sample of 67 drugs under two scenarios. First, what would sales revenues in those years have been if generic market share (for nonantibiotic drugs) were at its pre-1984 average? And second, what would sales revenues in those years be with a 2.8-year patent extension and increased generic market share at the end of year 14, as is the case today?

From those two revenue streams, the change in profits in years 12 to 20 is calculated assuming a marginal cost of production equal to 25 percent of the brand-name wholesale price. That assumption is well grounded in the literature on the pharmaceutical industry.[3] Since the appropriate measure of returns is after-tax profits, a marginal tax rate of 35 percent is also applied. Thus, an increase in sales revenues of $1 would add 49 cents to after-tax profits in a given year.[4] The change in profits is then discounted to the date of market introduction using a real interest rate of

1. Henry Grabowski and John Vernon, "Returns to R&D on New Drug Introductions in the 1980s," *Journal of Health Economics* (1994); Grabowksi and Vernon, "Longer Patents for Lower Imitation Barriers: The 1984 Drug Act," *American Economic Review* (May 1986); and Congressional Budget Office, *How Health Care Reform Affects Pharmaceutical Research and Development* (June 1994).

2. Alison Masson and Robert Steiner, *Generic Substitution and Prescription Drug Prices: Economic Effects of State Drug Product Selection Laws* (Federal Trade Commission, 1985).

3. See, for example, Office of Technology Assessment, *Pharmaceutical R&D: Costs, Risks and Rewards* (February 1993), p. 79. Also see CBO, *How Health Care Reform Affects Pharmaceutical Research and Development*, pp. 51-53.

4. Because (1 - 0.25)(1 - 0.35) = 0.49.

10 percent (consistent with previous studies that have measured the average returns from marketing new drugs).

Formulas

Because of the patent-term extensions available after 1984 and the delay between patent expiration and generic entry that existed before 1984, the sales streams in the two scenarios do not begin to diverge until year 14. The formula used for converting the difference between the pre- and post-1984 sales streams into profits (discounted to the date of market introduction) is:

$$\sum_{i=14-20} [(Pre84revenues_i - Post84revenues_i) * (1 - 0.25)(1 - 0.35)] \frac{1}{(1+r)^i}$$

where

i = the year on the market
r = a discount rate of 10 percent
0.25 = unit cost as a proportion of price
0.35 = the marginal tax rate

To obtain the pre- and post-1984 streams of sales revenues, an assumption is needed about the rate at which those revenues would erode without generic entry. For both streams, sales revenues were assumed to decline gradually starting in year 14 because of competition from other, improved innovator drugs. That erosion rate was assumed to be 6 percent in year 14 and to increase by 2 percentage points each year thereafter. The formula for sales revenue erosion caused by competition from other innovator drugs starting in year 14 is:

$$PreGenericRevenues_i = [PreGenericRevenues_{i-1}] * [1 - 0.06 - 0.02\ (i-14)]$$

That revenue stream is then further reduced depending on the size of the generic market. The bigger the generic market share, the smaller will be the sales revenues for the average innovator drug. The formula used to project the revenue stream, accounting for generic entry, is:

$$Revenues_i = (PreGenericRevenues_i) * (1 - GenericMarketShare_i)$$

Generic Market Share Before 1984

Before the Hatch-Waxman Act, generic market share was very small for most multiple-source drugs, with the exception of antibiotics. Generic market share averaged just 12.7 percent for 29 multiple-source drugs that were among the top 100, rated by total U.S. sales revenues, in 1980.[5] Those were drugs for which generic entry had occurred, however. Actual generic market share for the average brand-name drug before 1984 was smaller than that after accounting for cases in which generic entry did not occur.

Besides generic market share being small, the probability of generic entry was low for an off-patent brand-name drug before 1984. After excluding antibiotics and drugs approved before 1962, only 35 percent of the remaining top 200 drugs had generic versions available in 1983.[6] A few of those drugs had had their patent expire in 1980 or later; hence, the overall probability of generic entry at the average time it occurred (three years after patent expiration) was assumed to be slightly higher, 40 percent (see Table C-1). As a result, average generic market share for all multiple-source drugs was assumed to be 5.1 percent (40 percent of 12.7 percent), although that figure would be a bit smaller in the first year after generic entry.

5. The 12.7 percent average was calculated based on Table A5-1 in Masson and Steiner, *Generic Substitution and Prescription Drug Prices*. The sample in that report contained 45 multiple-source drugs. Ten were antibiotics, and six others were eliminated because they were still under patent, had minimal generic sales, or were only available under a generic name.

6. Grabowski and Vernon, "Longer Patents for Lower Imitation Barriers," pp. 195-198.

Table C-1.
Assumptions Used to Calculate the Change in Returns from Marketing a Drug

Assumption (For an average brand-name drug)	Before Hatch-Waxman Act	After Hatch-Waxman Act
Length of Patent Protection	11 years	13.8 years
Time Between Patent Expiration and Generic Entry	3 years	1.2 months[a]
Probability of Generic Entry	40 percent	91.5 percent
Generic Market Share		
1 year after generic entry	2.4 percent	40 percent
2 years after generic entry	5.1 percent	50 percent
3 or more years after generic entry	5.1 percent	60 percent

SOURCE: Congressional Budget Office.

a. This average does not account for cases in which generic entry was delayed. Such cases are taken into account in the estimated probability of generic entry.

Generic Market Share After 1984

CBO assumed that in the post-Hatch-Waxman period, generic entry normally occurs within 1.2 months of patent expiration. That figure resulted from examining 17 top-selling nonantibiotic drugs whose patents expired between 1990 and 1993. For 14 of those drugs, the average delay between patent expiration and generic entry was just over one month. (The date of generic entry for those drugs was included in a paper by Grabowski and Vernon; CBO obtained the date of patent expiration from the Food and Drug Administration's so-called *Orange Book* for 1990).[7] For the other three drugs, generic entry took 17 to 21 months after patent expiration; but according to an official of the Food and Drug Administration (FDA), that delay occurred largely because the agency was unable to evaluate those applications quickly since it was recovering from a scandal in the generic drug industry.[8]

CBO's assumption about the size of the generic market shortly after patent expiration and generic entry is based on an analysis of 21 innovator drugs in the retail pharmacy data set that first faced generic competition between 1991 and 1993. Generic sales constituted an average of 44.2 percent of total prescription sales for those drugs during the first full calendar year after generic entry.[9] Since that figure is based only on cases in which generic entry occurred, CBO adjusted it by the estimated probability of such entry—calculated to be 91.5 percent (see Box C-1). As a result, the average generic market share in the year following patent expiration, accounting for cases in which generic entry does not occur, is estimated to be about 40 percent.

By the time three years have elapsed since generic entry, the average generic market share for a drug is assumed to have reached 60 percent. CBO estimated that figure as follows. Overall generic market share —calculated as the volume of generic countable units sold to all purchasers in the United States divided by the volume of all drugs sold, including single-source drugs—was 40.4 percent in 1994, according to IMS America. (Note that this figure for 1994 generic market share is lower than the 50.5 percent figure in Box C-1 because it is taken as a percentage of all drug sales rather than just sales of multiple-source drugs.) Based on the retail pharmacy data set, CBO estimated that including all dosage forms in that average, rather than just those that are easily countable, such as tab-

7. See Henry Grabowski and John Vernon, "Longer Patents for Increased Generic Competition in the U.S." *PharmacoEconomics* (1996), Table 1, p. 112; and Department of Health and Human Services, Food and Drug Administration, *Approved Drug Products with Therapeutic Equivalence Evaluations* (1990). The patent expiration dates are also available at http://www.fda.gov/cder/da/ patex17.htm.

8. Personal communication with an FDA official on March 26, 1998.

9. The unweighted average generic market share for the 21 drugs was 43 percent. Weighting that average (a volume measure) by the value of the drugs' retail pharmacy sales revenues in 1991 (thus giving higher-selling drugs a greater emphasis) yields an average generic market share of 44.2 percent.

Box C-1.
Calculating the Probability of Generic Entry

Not every brand-name prescription drug with an expired patent faces competition from generic copies. In some cases, generic entry is delayed or even prevented because generic manufacturers have particular difficulty proving bioequivalence. Premarin, a drug to help prevent osteoporosis, is one such case. Since not all of the key ingredients in Premarin have been clearly identified, bioequivalence is hard to demonstrate.[1] Although the patent for Premarin has expired, no generic versions are currently available. Premarin was the 11th-best-selling drug in the United States in 1997, with sales of $800 million.[2] A few manufacturers obtained approval from the Food and Drug Administration (FDA) for generic copies of Premarin, but that approval was later withdrawn.

Generic entry can also be delayed when a drug contains a very potent active ingredient that is dangerous if the body absorbs too much too quickly. Generic manufacturers have more difficulty obtaining FDA approval for such drugs, so fewer generic manufacturers may apply for approval. The immunosuppressive drug Imuran (whose chemical name is azathioprine) is an example. Although Imuran lost patent protection in 1979, a generic version was not approved by the FDA until 1996.[3] Generic entry can also be delayed because of lawsuits between innovator and generic firms over which patents actually protect a drug.

To fully account for cases in which generic entry is prevented or delayed, the Congressional Budget Office examined the patent and exclusivity status of all single-source drugs in its retail pharmacy data set in 1994 (277 drugs) to determine what was preventing generic entry. Patent protection or an exclusivity provision prevented generic entry for all but 77 drugs. Of those 77, only eight had significant sales through retail pharmacies (of $40 million a year or more).[4] Two other important cases, Premarin and Coumadin (an anticoagulant), had modest generic retail sales in 1991, but those sales tapered off to an insignificant amount by 1994.[5]

Accounting for the 77 cases without generic competition, plus the cases in which such competition was severely limited, lowers the average generic market share in 1994 from 55.2 percent to 50.5 percent.[6] Thus, the implied probability of generic entry—adjusting generic market share (calculated as a percentage of the volume of sales of all multiple-source drugs) to account for cases in which generic entry does not occur soon after a drug's patent has expired—is 91.5 percent.[7] The higher percentage, 55.2 percent, was calculated by dividing the number of generic prescriptions dispensed by the total number of prescriptions dispensed for all multiple-source drugs with generic sales of $100,000 a year or more. To obtain the lower percentage, 50.5 percent, the calculation included in the denominator the number of prescriptions dispensed for off-patent brand-name drugs with no generic entry as well as for multiple-source drugs with any generic competition (including those with generic sales of less than $100,000).[8]

The estimate of 91.5 percent may not accurately reflect the probability of generic entry in the first year after patent expiration. That estimated probability is based on the overall market average and does not focus on drugs that lost their patent protection recently. Still, the cases in which generic entry does not occur are extremely limited for top-selling drugs and will not be accurately picked up if only a small number of drugs that recently lost patent protection are analyzed. The best approximation available was to take an overall market average. Applying that probability reduces generic market share in the first year after patent expiration from 44.2 percent to 40 percent. The sensitivity analysis discussed later in this appendix shows that CBO's estimate of the decline in returns is only slightly sensitive to reasonable variations in the assumed level of post-1984 generic market share.

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1. "Wyeth-Ayerst Commits to Characterization of Premarin, FDA Says; Generic Conjugated Estrogens May Not Be Approved Until Premarin Is Characterized," *The Pink Sheet*, F-D-C Reports, May 12, 1997, p. 3.

2. "Post-1990 Launches Represent 43% of Rx Market, IMS Says," *The Pink Sheet*, F-D-C Reports, March 9, 1998, p. 9.

3. Personal communication with an FDA official, March 31, 1996. (The patent expiration date was obtained from a data set provided by David Dranove of Northwestern University.)

4. In 11 cases, drugs with annual retail sales through pharmacies that totaled $11 million to $33 million did not have generic copies. The remaining cases had sales of less than $10 million; many had sales of less than $1 million. Of the eight significant drugs with no generic competition in 1994, six now have generic competitors. One drug that still has no generic competitors is the birth control pill Lo/Ovral. The patent status of two other birth control pills in the data set that had sales of more than $50 million a year and no generic competition could not be determined, so they were not included in calculating the probability of generic entry.

5. Generic competition for Coumadin has been hampered. See "Barr Is Barring Warfarin Competitors with Bulk Agreement, Invamed Sues," *The Pink Sheet*, F-D-C Reports, March 2, 1998, p. 11; and "Dupont Merck Payments to PBMs Blocked Barr Warfarin Dispensing," *The Pink Sheet*, F-D-C Reports, March 16, 1998, p. 26. Generic sales for Coumadin dropped between 1991 and 1994 because the two previously approved generic drugs' manufacturers were forced to leave the market during a scandal involving certain generic drug manufacturers and FDA officials in the late 1980s.

6. That generic market share is calculated for all dosage forms. Confining the dosage forms only to tablets and capsules increases generic market share by 2.2 percentage points.

7. Because 50.5 divided by 55.2 equals 0.915.

8. The only brand-name drugs with retail pharmacy sales of over $20 million that had competing generic retail pharmacy sales of less than $100,000 were Premarin and Coumadin. Both of those were top-selling brand-name drugs.

Table C-2.
Formulas for Calculating Generic Market Share

Year of Drug's Product Life	Before Hatch-Waxman Act		After Hatch-Waxman Act	
	Formula[a]	Value	Formula[b]	Value
14	None	0	(0.44)(0.915)(0.1)	0.04
15	(0.06)(0.4)	0.024	(0.44)(0.915)(0.9) + (0.5)(0.1)	0.41
16	(0.127)(0.4)	0.051	(0.5)(0.9) + (0.6)(0.1)	0.51
17 to 20	(0.127)(0.4)	0.051	(0.6)	0.60

SOURCE: Congressional Budget Office.

a. Equal to average generic market share when generics are available times the probability of generic entry.

b. Equal to average generic market share times the fraction of the year to which the average applies. For example, in year 15, the formula is a weighted average of the average generic market share in the first and second years after patent expiration.

lets and capsules, reduces generic market share to 38.2 percent.[10] To calculate average generic market share for drugs that have been off patent for three or more years, the 38.2 percent figure was divided by 66.7 percent, the share that off-patent drugs constituted of the retail pharmacy data set in 1994. As a result, CBO estimated that generic sales represented 57.3 percent of all sales of multiple-source and off-patent single-source drugs in 1994.[11] Since generic market share has continued to increase slightly since 1994, and since older drugs would have a slightly higher generic share than the market average (which includes drugs that recently went off patent), CBO adjusted that estimate of average generic market share upward to 60 percent.[12]

The figure for generic market share in the second year after patent expiration, 50 percent, is simply an average of the figures for the first and third years.

In CBO's calculations of generic market share, the estimated probability of generic entry (91.5 percent) helps to account for the cases in which generic entry is delayed by a year or more. In the first year following patent expiration, generic market share equals 44.2 percent multiplied by 91.5 percent, or 40 percent. In the third year after patent expiration and later, the cases in which generic entry did not occur were incorporated into the calculation of a generic market share of 60 percent. How sensitive CBO's calculation of the change in returns from marketing is to those estimated generic market shares is analyzed below.

The formulas used to project generic market share based on this analysis are shown in Table C-2. The first year of patent expiration is split between years 14 and 15 of a drug's product life. Since generic entry is assumed to occur at the very end of year 14, in that year generic market share is equal to only 10 percent of 44.2 percent multiplied by 91.5 percent, which is 4 percent. In year 15, generic market share is a weighted average of generic market share in the first year after patent expiration (90 percent) and the sec-

10. Limiting the calculation only to tablets and capsules raises the average generic market share calculated from the retail pharmacy data set by 2.2 percentage points.

11. That figure has already been adjusted to account for cases in which generic entry was prevented, since the sales of single-source, off-patent brand-name drugs were accounted for in the 66.7 percent.

12. IMS America estimated that overall generic market share in 1996 was 42.6 percent. Adjusting that figure from mainly tablets and capsules to all dosage forms would imply a market share of 40.4 percent. Then, assuming the same split between brand-name and generic drugs in 1996 as in 1994 would yield a generic market share of 60.5 percent for drugs off patent.

ond year after patent expiration (10 percent). The average generic market share for year 15 is therefore 41 percent.

Sensitivity Analysis

CBO examined the sensitivity of its estimate of the decline in the present discounted value of the average returns from marketing a new drug ($27 million) to the assumptions used to construct the pre- and post-1984 streams of sales revenues. The results indicate that the estimate is little affected by modest changes in the key assumptions (see Table C-3).

If, in constructing the pre-1984 sales stream, CBO assumed that generic drugs took four years instead of three to enter the market after patent expiration, the estimated decline in returns would be $28 million, just $1 million different. That change is small because the size of the pre-1984 generic market was small, so postponing generic entry by another year in that period does not have much effect on the basic result.

The effect would be greater if generic entry was further postponed in the post-1984 period (since generic market share is higher then), but the data that underlie CBO's estimate of a 2.8-year average postponement under the Hatch-Waxman Act are solid. If the average length of a patent extension was six months shorter, returns would fall by an additional $5 million. If the average length was six months longer, the decline in returns would be $4 million less. However, the data on patent-term extensions obtained for all drugs approved between 1992 and 1995 make it unlikely that the estimated average length of an extension would be off by as much as six months.

CBO's basic result is not very sensitive to a small increase in the size of the generic market. For example, if the post-1984 generic market share was 45 percent in the first year after generic entry, rising to 65 percent in the third year and beyond, the decline in returns would be $30 million—only $3 million more than the base case. Those alternative assumptions are based on what might be a reasonable upper bound for current levels of generic market share.

CBO assumed that the marginal cost of producing another unit of a prescription drug was 25 percent of its brand-name price. Varying the marginal cost from 20 percent to 30 percent of the brand-name price causes the total decline in returns to vary between $25 million and $29 million. Thus, CBO's estimate is not particularly sensitive to reasonable variations in incremental unit costs.

As a drug becomes obsolete and its efficacy is surpassed by that of newer innovator drugs, its sales revenues gradually erode. That erosion rate was assumed to be 6 percent in year 14 and 8 percent in year 15, increasing by 2 percentage points each year thereafter. If CBO had used a slightly slower rate of revenue erosion caused by product obsolescence—starting at 5 percent in year 14 and increasing by 1 percentage point each subsequent year—the total decline in returns would be an estimated $30 million. By contrast, with a faster erosion rate—6 percent in year 14, increasing by 3 percentage points each year thereafter—returns would decline by $25 million. Hence, the estimate is fairly robust to that assumption as well.

As discussed in Chapter 3, the extent to which brand-name prices respond to generic entry is unclear from previous studies. CBO's base case assumes that those prices do not respond to generic entry. If brand-name prices did change because of generic competition, they would primarily affect the profit stream in the post-1984 scenario, since generic market share was so small before 1984. If, because of increased discounting, the average brand-name price was 5 percent lower in each year after generic entry in the post-1984 scenario, the returns from marketing a new drug would fall by $29 million, a difference of $2 million. If, conversely, the average brand-name price was 5 percent higher in that period after generic entry, estimated returns would fall by $25 million. Thus, CBO's calculation is not highly sensitive to any effect that generic entry might have on brand-name prices.

An important number on which the calculation depends is sales revenues in year 13 (the average

Table C-3.
How Sensitive Is the Calculation of Returns to Changes in the Base-Case Assumptions?

Base-Case Assumption	Alternative Assumptions	Decline in Returns (Millions of 1990 dollars) Total Decline	Decline in Returns (Millions of 1990 dollars) Variation from Base Case[a]
Pre-1984 Delay Between Patent Expiration and Generic Entry			
3 years	4 years	28	1
	2 years	26	-1
Length of Hatch-Waxman Patent-Term Extension			
2.8 years	6 months longer	23	-4
	6 months shorter	32	5
Post-1984 Generic Market Share After Generic Entry			
40 percent one year later, 50 percent two years later, 60 percent three or more years later	Higher: 45 percent one year later, 55 percent two years later, 65 percent three or more years later	30	3
	Lower: 35 percent one year later, 45 percent two years later, 55 percent three or more years later	24	-3
Marginal Cost			
25 percent of unit price	20 percent of unit price	29	2
	30 percent of unit price	25	-2
Sales Erosion Rate from Brand-Name Competition			
6 percent in year 14, increasing by 2 percentage points each year thereafter	Higher: 6 percent in year 14, increasing by 3 percentage points each year thereafter	25	-2
	Lower: 5 percent in year 14, increasing by 1 percentage point each year thereafter	30	3
Post-1984 Change in Brand-Name Prices Because of Generic Entry			
No price change	Brand-name price is 5 percent higher in years 14 to 20	25	-2
	Brand-name price is 5 percent lower in years 14 to 20	29	2

SOURCE: Congressional Budget Office.

a. The base case is a $27 million decline in the present discounted value of returns.

drug's peak year, before product obsolescence and generic entry occur). According to CBO's data set, those revenues averaged $139.2 million in 1990 dollars.[13] CBO's estimate of the change in returns is not very sensitive to modest changes in those revenues. For example, if sales revenues in year 13 were 10 percent lower, the estimated decline in returns would be $24 million. If sales revenues in year 13 were 10 percent higher, the estimated decline in returns would be $30 million. Of course, if revenues were 10 percent lower or higher in all years leading up to year 13, then total returns would also be lower or higher than the assumed $210 million to $230 million. But even accounting for the corresponding change in total returns, the result (taken as a percentage of the total expected returns from marketing a new drug) would remain a decline of about 12 percent, on average.

13. Average U.S. sales for the 67 drugs in CBO's sample were $139.2 million in year 11 and were assumed to continue at that level through year 13.

Appendix D

The Replacement Effect

Besides its primary effect of reducing the returns from marketing innovator drugs, generic entry can also have a small positive effect on the incentive to innovate. Economists have shown that a monopolist can have a tendency to "rest on his laurels."[1] Monopolists may have little incentive to research and develop new products that will compete directly with their currently marketed products—a phenomenon referred to as the replacement effect. When a cash flow model of the expected returns from marketing an innovative product incorporates that effect, it shows that in a few cases, the net impact of generic entry on a monopolist's incentives to innovate could be close to zero (although in general one would expect returns to decline). In those cases, generic entry may reduce the size of the replacement effect almost as much as it reduces the present discounted value of the returns from marketing an innovation.

Whether the reduced replacement effect significantly offsets the direct decline in returns caused by generic competition will depend on how much of the current product's market is being replaced and the timing of that replacement. The reduction in the replacement effect is more likely to be an important factor when the product being replaced is within a few years of patent expiration. That implies that when pharmaceutical companies invest in developing new drugs in therapeutic classes in which they are already market leaders, the rise in generic competition may not lower their incentive to innovate as much as the Congressional Budget Office's (CBO's) calculation of the returns from marketing a drug (presented in Chapter 4) would appear to indicate.

Still, only a limited number of cases exist in which the reduced replacement effect could be strong enough to nearly offset the direct decline in returns because of generic competition. Although companies do continue to develop drugs in therapeutic areas where they are market leaders, they also invest in therapeutic areas where few treatments exist. And it is in precisely those areas—where patients may benefit the most from a new drug—that the offsetting replacement effect is not present at all.

As Box D-1 shows, the profit stream from innovating is equal to the present discounted value of the returns from marketing the innovation, offset by any decline in the present discounted value of the profit stream from the currently marketed product (that decline, shown in brackets in the box, represents the replacement effect). Generic entry reduces the present discounted value of the returns from marketing the innovation (by an average of $27 million in 1990 dollars, according to CBO's analysis) but is offset somewhat by a decrease in the replacement effect.

That relationship can be expressed mathematically, as follows. Assuming that:

t = number of years a product has been on the market

t_g = year of generic entry

1. Jean Tirole, *The Theory of Industrial Organization* (Cambridge: MIT Press, 1988), p. 392, quoting Kenneth J. Arrow. Although manufacturers of brand-name drugs usually do not have a pure monopoly, the analysis still applies to innovation in this industry.

Box D-1.
Calculating the Impact of the Replacement Effect and Generic Competition on the Returns from Innovation

Calculation of Returns from Innovation When New Products Replace Old Ones

Present Discounted Value (PDV) of Profits from Innovation	=	PDV of Returns from New Product	–	[PDV of Returns from Currently Marketed Product	x	Share of Current Market Replaced by New Product]

Calculation of How the Rise in Generic Entry Since 1984 Has Affected Returns

Change in PDV of Profits from Innovation Caused by Increased Generic Entry	=	Change in PDV of Returns from New Product	–	[Change in PDV of Returns from Currently Marketed Product	x	Share of Current Market Replaced by New Product]

T = number of years of product life

h = year in the life of the currently marketed product when a new, competing product is introduced by the monopolist

α = share of the current product's market that is absorbed by the new product

$\Pi^M(t)$ = monopolist's profits in year t with no generic entry

$\Pi^G(t,t_g)$ = monopolist's profits in year t with generic entry

$\Pi^C(t,t_g)$ = $\Pi^M(t)$ if $t < t_g$
$\Pi^G(t)$ if $t \geq t_g$

V^M = profit stream generated from introducing a new product after the current product has been on the market for h years, in the absence of generic competition following patent expiration

V^G = profit stream generated from introducing a new product after the current product has been on the market for h years, with generic entry in year t_g

It is assumed that the functions $\Pi^M(t)$ and $\Pi^G(t,t_g)$ are the same for the product that is currently on the market as for the new one. Those functions could be thought of as the average profits generated from marketing a new drug t years after market introduction. In the absence of generic entry, the change in the profit stream from introducing a new product after the current one has had h years on the market is equal to:

$$V^M = \sum_{t=1}^{T} \Pi^M(t)\left(\frac{1}{1+r}\right)^t - \alpha \sum_{t=h}^{T} \Pi^M(t)\left(\frac{1}{1+r}\right)^{t-h}$$

The first term equals the present discounted value of the profits from the innovation. The second term equals the decline in the present discounted value of the profit stream of the currently marketed product after the innovation is introduced (the replacement effect). After accounting for generic entry, the profit stream from innovation becomes:

$$V^G = \sum_{t=1}^{t_g} \Pi^M(t)\left(\frac{1}{1+r}\right)^t + \sum_{t=t_g}^{T} \Pi^G(t)\left(\frac{1}{1+r}\right)^t - \alpha \sum_{t=h}^{T} \Pi^C(t)\left(\frac{1}{1+r}\right)^{t-h}$$

The first two terms are equal to the present discounted value of the profits from the innovation. The second term accounts for lower postpatent revenues when generic entry occurs. Together, those equations imply that the effect of generic entry on the returns from marketing an innovation can be expressed as:

$$V^M - V^G = \sum_{t=t_g}^{T} [\Pi^M(t) - \Pi^G(t)]\left(\frac{1}{1+r}\right)^t - \alpha \sum_{t=h}^{T} [\Pi^M(t) - \Pi^C(t)]\left(\frac{1}{1+r}\right)^{t-h}$$

The first term in that combined equation equals the fall in the present discounted value of the profit stream from the innovation because of generic entry starting in year t_g. The second term equals the loss in the future profit stream from the currently marketed product because its sales volume declines after the more innovative product is introduced. The amount by which V^M exceeds V^G is diminished by the change in the replacement effect.

Note that using present discounted values diminishes the first term more than the second term. The effect of generic entry on the current profit stream is diminished because it occurs at the end of a drug's product life. But the change in the replacement effect under generic entry occurs sooner, as reflected by discounting by $t - h$ years rather than by t years. Suppose that $h = 10$, so that a new product is introduced after the monopolist's current product has been on the market for 10 years. The model used in this study estimates that the effect of generic entry on the present discounted value of profits, when discounted back only to year 10, is more than twice the value when discounted back to year 0. If more than half of the current product's market is absorbed by the new product ($\alpha > 0.5$), the change in the replacement effect would completely offset the first term. The change in the replacement effect is largest when the currently marketed product approaches patent expiration.